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Biomedical Research Division Significant Accomplishments for FY 1983



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Biomedical Research Division Significant Accomplishments for FY 1983

Norman V. Martello, Nelson and Johnson Engineering, Inc.

Prepared for
Biomedical Research Division
Ames Research Center

February 1984



National Aeronautics and
Space Administration

Ames Research Center
Moffett Field, California 94035

N84-20128 #

TABLE OF CONTENTS

INTRODUCTION.....	1
Organization of the Biomedical Research Division.....	5
Civil Service Personnel in the Biomedical Research Division...	6
 1. THE OPERATIONAL MEDICINE PROGRAM IN NASA.....	9
Longitudinal Studies.....	11
Crew Health Maintenance.....	17
Space Adaptation Syndrome.....	25
 2. THE BIOMEDICAL RESEARCH PROGRAM IN NASA.....	31
Cardiovascular Deconditioning.....	33
Basic Mechanisms of Space Motion Sickness.....	43
Bone Alterations.....	65
Muscle Atrophy.....	77
Fluid and Electrolyte Changes.....	89
Biological Effects of Particle Radiation.....	97
Human Behavior and Performance.....	103
General Biomedical Research.....	109
 3. THE GRAVITATIONAL BIOLOGY PROGRAM IN NASA.....	119
Developmental Biology.....	121
Biological Adaptation.....	129
 4. LIFE SCIENCES FLIGHT EXPERIMENTS PROGRAM IN NASA.....	141
STS-8 Activities and Experiments.....	145
Cosmos 1514 Experiment.....	147
Spacelab 2 Experiment.....	148
Spacelab 3 Activities and Experiments.....	148
Spacelab 4 Experiments.....	149

5.	ADDITIONAL ACTIVITIES.....	153
	Electron Microscopy and Plant Research.....	154
	Director's Discretionary Funding.....	158
	Appointments and Awards.....	159
	Lectures, Meetings and Workshops.....	162
	Thesis Committees.....	167
	Seminar Speakers Invited by the Biomedical Research Division in FY 1983.....	168
6.	FACILITIES.....	171

INTRODUCTION

The Biomedical Research Division (LR) at Ames Research Center, near San Francisco, California, continued to serve NASA and the scientific community as the primary organization for basic research in space medicine and biology during fiscal year 1983. Our efforts in basic R&D covered a wide range of disciplines in the biological and behavioral sciences. Using both animal and human subjects, investigators examined the adaptation of various organisms and organ systems to the effects of the aerospace environment. To assure astronaut health and productivity in such environments required the study of physiological functions under the effects of acceleration, radiation and weightlessness. Comparing data from actual flight in space to that from ground-based simulations, such as bedrest with humans, provided new insights into physiological changes during flight.

The English naturalist and theorist Charles Darwin noted that we could not experimentally remove the force of gravity on Earth, and he envisioned the importance of sensitivity to gravity as a factor in biological development, function and evolution. Spaceflight made research feasible in an environment virtually free from the influences of gravity. Thus, NASA's programs in the life sciences at LR benefitted both the scientific and aerospace communities through: (1) research to ensure the health and performance of humans in space (Operational Medicine Program), (2) basic research to investigate major physiological and psychological challenges to humans in space, research which is also applicable to problems facing the health care community on Earth (Biomedical Research Program), and (3) research to understand the nature of life itself, particularly the role of gravity on the development and evolution of Earth's creatures (Gravitational Biology Program). These and other Life Sciences Programs were administered from NASA Headquarters in Washington, D.C. to the Ames Research Center, Johnson Space Center, the Jet Propulsion Laboratory, and other centers to maintain safe and successful Space Shuttle flights. Specifically in the Biomedical Research Division at Ames, the principal research objectives were:

- o to identify and understand physiological changes occurring during and after manned spaceflight;
- o to develop countermeasures to untoward physiological changes occurring during spaceflight;
- o to broaden the population base of individuals eligible to fly in space by determining the effects of age, sex, physical conditioning, and clinical disease on an individual's ability to withstand the rigors of spaceflight;
- o to use the unique environment of spaceflight to understand the basic biological processes that cannot be effectively studied on Earth;
- o to develop and use techniques to simulate the effects of hypogravity, or weightlessness, for research in space medicine and biology; and
- o to develop biomedical instrumentation for application to research problems in space medicine and biology.

Results from manned flight over the past year present new challenges for the Life Sciences in NASA. With the completion of the initial missions of the Space Transportation System (STS), or Space Shuttle, it is now recognized that astronauts must perform increasingly complex and demanding tasks in the weightless environment as well as skillfully pilot the Shuttle under the effects of reentry acceleration. Successful adaptation to the space environment ensures the safe and productive use of short-duration Shuttle flights, and the scientific and economic growth concomitant with the establishment of long-duration space stations.

During FY 1983 research at LR was conducted through a combination of intramural projects, using the specialized laboratories and aerospace test facilities at Ames, and extramural projects, contributing the talents of outside investigators from universities, medical schools, hospitals, and research institutes. Thirty-six in-house investigators performed 40% of all research activities, and coordinated the remaining 60%, which was conducted by outside institutions. The National Research Council's Post-Doctoral Fellowships, which are held generally for two-year periods, provided eight talented researchers in cardiovascular, skeletal and neural research. Four researchers also worked as detailees from the U.S. Air Force. Senior scientists of LR reported to NASA Headquarters on each unique research area through Research Technology Objectives and Plans (RTOPs), which are summarized in the following report.

Two Assistant Division Chiefs maintained close contact with the Program Managers at NASA Headquarters and with the Office of the Director of the Life Sciences at Ames, as well as coordinated the efforts of the Biomedical Research Division. The Assistant Chiefs consulted with and received guidance from the Division Chief, Harold Sandler, M.D., to direct the overall research. This year NASA awarded Dr. Sandler with the Space Agency's first Senior Executive Services Sabbatical on the basis of his internationally recognized contributions in cardiovascular research and the

biomedical effects of extended duration spaceflight. Dr. Sandler spent his sabbatical at the nearby Stanford University School of Medicine, where he worked as a Visiting Professor of Medicine.

The Division's staff includes a combination of Civil Service personnel and university collaborators, both on-site and off-site, in 14 RTOP areas. LR's complement of 37 civil servants include 16 Ph.D.s, one D.V.M., two M.D.s, seven Masters and eight Bachelors level personnel engaged in biomedical and space biology research. On the staff are internationally recognized experts in the fields of biochemistry, endocrinology, cardiovascular physiology, environmental physiology, exercise physiology, gerontology, neuroanatomy, and bone mineral metabolism. The Division staff members possess expertise in pharmacology, vestibular function, experimental pathology, immunology, radiation biology, biorhythms, behavior and performance, psychology, the biochemistry of proteins, carbohydrates and lipids, and gravitational biology.

Research and development on the ground also contributed to LR's participation in flight experiments performed in support of the Space Shuttle program, and on the latest in a series of joint US-USSR biological spaceflights, the unmanned biosatellite, Cosmos 1514, launched by the Soviet Union. Echocardiography (ultrasound) studies were conducted on Shuttle crew members before and after flight, which will lead ultimately to obtaining cardiovascular data during flight.

To help the dissemination of scientific information and expertise, the research facility at Ames also provided a valuable training ground for 30 students, including 12 graduate students involved in thesis work directly applicable to the Division's current research projects. Such opportunities contributed to the training of skilled investigators to meet the continuing needs of advanced aerospace research at a time when the first generation of space biologists and psychologists are approaching retirement. LR scientists also provided NASA Headquarters with scientific review of new research proposals, and participated in a wide variety of scientific committees, working groups and advisory teams. Additional effort was initiated to integrate and present research findings in a useful fashion for review by NASA Headquarters, by review committees of the American Institute of Biological Sciences (AIBS), and by the biological, medical and aerospace communities in general. The descriptions that follow include results of research conducted by all Principal Investigators in the Division, as well as the research conducted by universities and private industry, which was sponsored by NASA and monitored by personnel of the Biomedical Research Division at Ames. Further information on the programs of the Biomedical Research Division can be obtained by contacting any of the following individuals:

Harold Sander	Kenneth A. Souza	Malcolm M. Cohen
Division Chief	Assistant Division Chief	Assistant Division Chief
Mail Stop 239-8	Mail Stop 239-17	Mail Stop 239-7

Ames Research Center, Moffett Field, California 94035

TABLE I. ORGANIZATION OF THE BIOMEDICAL RESEARCH DIVISION

Harold Sandler, Chief

Doris M. Furman, Secretary

Anne L. Goodwin, Technical Assistant

Kenneth A. Souza, Assistant Chief

Malcolm M. Cohen, Assistant Chief

Carolyn L. Wilson, Secretary

Rita L. Marks, Secretary

PROGRAM RESPONSIBILITIES

PROGRAM RESPONSIBILITIES

Cosmos & Spacelab Flight Experiments

Space Shuttle Experiments

Gravitational Biology
developmental biology
biological adaptation

Operational Medicine
longitudinal studies
crew health maintenance
space adaptation syndrome

Biomedical Research
bone alterations
muscle atrophy
radiation effects & protection

Biomedical Research
cardiovascular deconditioning
space motion sickness
fluid & electrolyte changes
behavior and performance
general biomedical research

Management
facilities
safety
property

Management
Office of Applications for
Space Technology
Department of Defense programs

TABLE II. CIVIL SERVICE PERSONNEL IN THE BIOMEDICAL RESEARCH DIVISION

FUNCTION	BACKGROUND
<u>Administrative</u>	
D.M. Furman	clerical support to Division Chief
A.L. Goodwin	budget & logistics, medical technology, biochemistry, Division Technical Assistant
R.L. Marks	clerical support to Division administrators and personnel
C.L. Wilson	clerical support to Division administrators and personnel
<u>Behavior & Performance Research</u>	
M.M. Cohen	neurophysiology, psychology, Assistant Division Chief
C.W. DeRoshia	chronobiology
C.M. Winget	chronobiology, pharmacology, comparative physiology
<u>Bone Alterations Research</u>	
R.R. Adachi	analytical chemistry
H.J. Ginoza	genetics, physiology
E.M. Holton	bone and mineral physiology, pharmacology
D.R. Young	bone and mineral physiology
<u>Cardiovascular Deconditioning Research</u>	
J.W. Hart	animal care
H. Sandler	cardiovascular physiology, medical doctor, Division Chief
<u>Crew Health Maintenance Research</u>	
D.J. Goldwater	human physiology, medical doctor
<u>Gravitational Biology Research</u>	
R. Binnard	bacteriology, developmental biology, histology, insect physiology
B. Daligcon	physiology
J. Miquel	developmental biology, gerontology, histology, pharmacology
J. Oyama	gravitational physiology
K.A. Souza	embryology, space biology, Assistant Division Chief

Fluid and Electrolyte Research

J.V. Danellis	pharmacology, endocrinology
J.E. Greenleaf	environmental physiology
L.C. Keil	endocrinology

General Biomedical Research

C.B. Dolkas	physiology, insulin/glucose metabolism, biomedical engineering
A.D. Mandel	immunology, bacteriology
J.A. Williams	immunology

Muscle Atrophy Research

S. Ellis	biochemistry, muscle physiology
R.E. Grindeland	physiology
P.R. Lundgren	biochemistry, analytical chemistry

Radiation Effects and Protection Research

R.L. Corbett	electron microscopy, zoology
L.M. Kraft	radiobiology, veterinary medicine
D.E. Philpott	electron microscopy, radiobiology
M.J. Stevenson	biochemistry, histology

Space Motion Sickness Research

J.O. Coleman	neurophysiology, veterinary science
M.L. Corcoran	experimental & behavioral psychology
P.S. Cowings	psychophysiology, psychology
N.G. Daunton	neurophysiology, neuropsychology
W.R. Mehler	neuroanatomy

OPERATIONAL MEDICINE

THE OPERATIONAL MEDICINE PROGRAM IN NASA

The Operational Medicine Program is responsible for assuring the health, well-being and performance of astronauts and payload specialists while working in space. This crucial work, which is critical to mission success, is achieved through (1) clinical and preventive medicine programs and (2) operational research and development. The first activity requires the development and continuous update of astronaut medical selection and retention (annual) certification standards; pre and postflight medical examinations of STS crews; early detection, prevention and/or treatment of crew illness; biomedical training of space crews in emergency medical procedures; and training of NASA/DOD (Department of Defense) medical personnel in principles and practice of space medicine. These activities are primarily accomplished through the establishment and maintenance of specialized biomedical laboratories and offices at Johnson Space Center (JSC) in Houston and Kennedy Space Center in Florida. The second activity addresses medical operational issues and problems which have been encountered in the conduct of previous manned missions. This program includes acquisition of trend data to elucidate the time course of long-term effects from repeated exposures to the space environment; the development of health maintenance protocols (such as exercise, anti-cardiovascular deconditioning measures, space motion sickness predictors and/or drugs, etc.), procedures, equipment, and environmental monitoring for use during space missions; and simulations of STS flights that facilitate the testing and development of specific medical protocols on the ground prior to their use in space. These activities are conducted by JSC, Ames Research Center, and selected DOD or university research laboratories.

(From NASA Space Science and Applications Notice, October 25, 1982)

Arnauld Nicogossian
Director of NASA Life Sciences

LONGITUDINAL STUDIES

LONGITUDINAL STUDIES AMES RTOP 199-10-22
D.J. Goldwater, manager

The basic medical research performed at Ames Research Center (ARC) under this RTOP provides medical data from astronauts and control populations over periods ranging from months to years. Longitudinal, retrospective studies compare these two groups revealing the magnitude of physiological changes that occur during spaceflight. This research, then, helps to define postflight recovery programs for the health and career longevity of astronauts. Criteria for the initial selection of personnel for the astronaut corps is also updated as required.

During the past decade the Human Research Facility, managed by Dee O'Hara of the Biosystems Division at ARC, and the Stanford and VA Hospital clinical research centers were used to study over 180 males and females, spanning the ages of 19 to 65 years, under simulations of Space Shuttle flight stress. Subjects underwent bedrest horizontally (0°) and head down (-6°) to simulate many of the effects of weightlessness. Acceleration of +3 Gz (head to foot) on Ames' Human Centrifuge followed approximately a week of bedrest. (+1.2 Gz for 17 minutes is the typical acceleration force on humans during reentry of the Space Shuttle with the steepest reentry profile of +2.8 Gz.) In past US and USSR manned flights, astronauts flew through a reentry profile different and less stressful physiologically from that of the Space Shuttle. Space travellers returned to Earth on their backs, withstanding up to -6 Gx (chest to back) for brief periods. Bedrest followed by +3 Gz acceleration allowed ARC's flight surgeons to identify predictive factors affecting orthostatic tolerance (susceptibility to greyout, blackout, or fainting). Some of the factors contributing to low orthostatic tolerance included aerobic exercise, younger age, taller height, feminine gender, low resting blood pressure and heart rate, and low levels of plasma renin activity and plasma norepinephrine.

Echocardiography plays an important role in identifying the effect of reduced size and volume of the heart resulting from bedrest or spaceflight. Echocardiography uses high frequency sound waves, or ultrasound, to visualize the heart and its great vessels. An echocardiogram data base of over 200 healthy men and women was established for comparison with astronauts. A valuable exchange of information and collaboration with flight surgeons and biomedical researchers at Johnson Space Center is also ongoing.

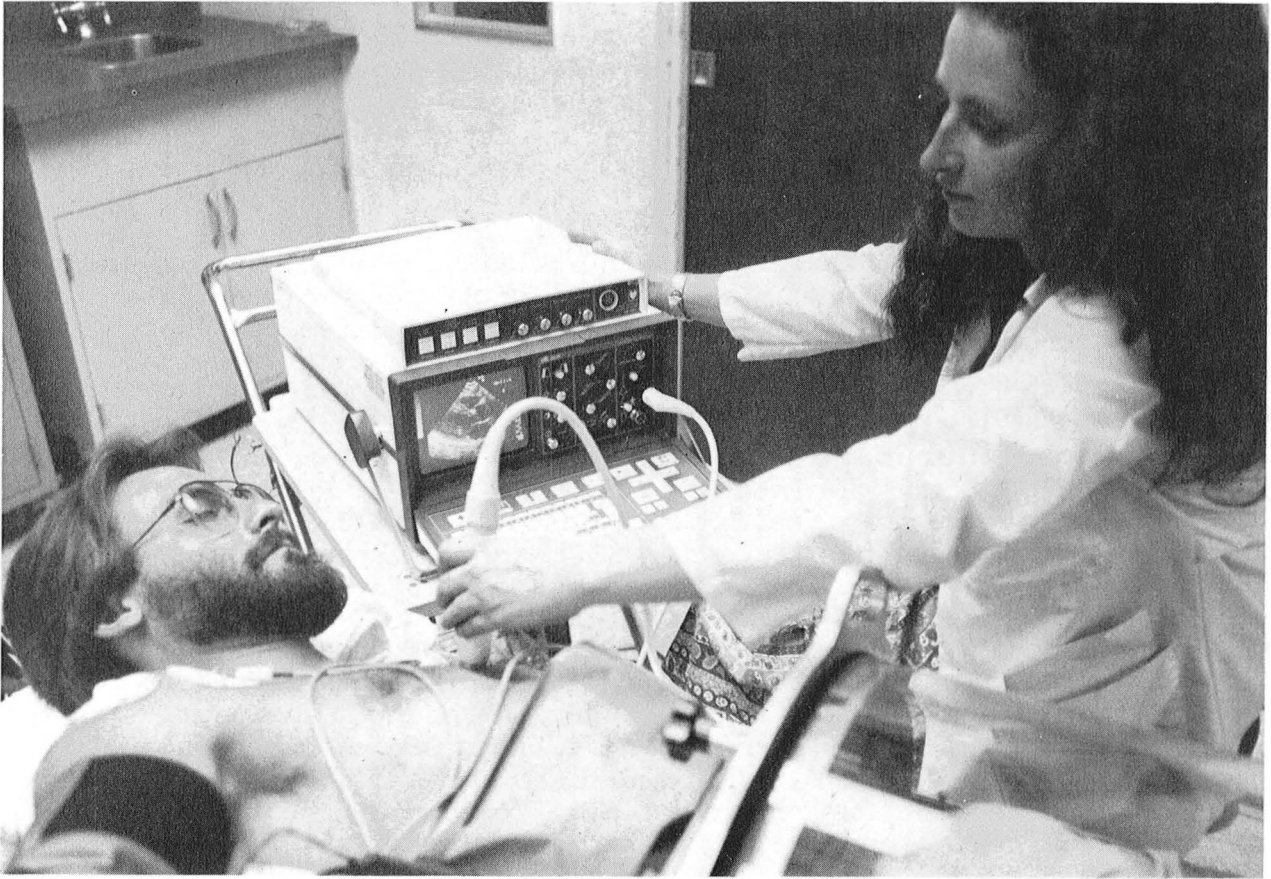


Fig. 1. The portable ADR ultrasonoscope is used to obtain a subject's echocardiogram during lower body negative pressure (LBNP) to assess orthostatic tolerance after bedrest, which simulates some of the effects of weightlessness. This unit will be used onboard the Space Shuttle in 1984. The unit fits easily into a Shuttle storage locker. (Popp 199-10-22-10)

R.L. Popp, Stanford University, School of Medicine
 D.J. Goldwater, Ames Technical Monitor

Echocardiograms were performed pre- and postflight on 17 Shuttle crew members from the STS-5 mission through STS-8, although thus far only seven astronauts were available for immediate postflight (L+0) exams. During L+0 exams, crews displayed an average 23% fall in end diastolic volume, a 28% decrease in stroke volume, and a 31% increase in resting heart rate. At seven to 14 days postflight, end diastolic volume was still depressed (-11%), but ejection fraction rose by 8.3% compared to preflight measures. Muscle thickness of the ventricular wall did not measurably decrease postflight. (These results indicate that cardiac output was maintained by a different mechanism immediately postflight compared to seven to 14 days later.) In addition, the persistent postflight decreases in cardiac filling volumes after these five to eight-day Shuttle flights were similar to previously reported echo results after the 84-day Skylab flight and also similar to the results of a ten-day bedrest simulation study in 19 to 65-year-old men. Echocardiograms were obtained with a portable ultrasonoscope (Fig. 1) which is being prepared for Shuttle flight in 1984.

Ground-based studies were also performed with 35- to 50-year-old men who underwent repeated bedrest (-6° head down) to simulate repeated Shuttle flights. Thousands of echo measurements were taken in these subjects during orthostatic stress (lower body negative pressure) with and without drugs that affect autonomic nervous system control and cardiac function. These echo measurements were conducted to determine whether cardiac function changes inflight and the precise mechanism of change. Echocardiograms also provide a means to verify ground-based (-6° bedrest) simulation compared to spaceflight.

Publications: (1) Gordon, E.P., I. Schnittger, P.J. Fitzgerald, P. Williams, and R.L. Popp. 1983. "Reproducibility of left ventricular volumes by two-dimensional echocardiography." JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY 2(3): 506-513. (2) Kantrowitz, N.E., I. Schnittger, A. Schwarzkopf, P.J. Fitzgerald and R.L. Popp. 1983. "Rapid, semiautomated technique for estimating left ventricular volume." AMERICAN HEART JOURNAL 106(3): 521-527. (3) Pollick, C., P.J. Fitzgerald, and R.L. Popp. 1983. "Variability of the digitized echocardiography: Size, source, and means of reduction." AMERICAN JOURNAL OF CARDIOLOGY 51(3): 576-582. (4) Schnittger, I., E.P. Gordon, P.J. Fitzgerald, R.L. Popp. 1983. "Standardized intracardiac measurements of two-dimensional echocardiography." JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY 2(5): 934-938.

CREW HEALTH MAINTENANCE

CREW HEALTH MAINTENANCE AMES RTOP 199-10-32
D.J. Goldwater, manager

Over the past decade the Human Research Facility at Ames Research Center tested over 180 male and female subjects under head-down (-6°) and horizontal (0°) bedrest to simulate the deconditioning effects that occur during the weightlessness of spaceflight. Scientific experiments were devised to achieve medical techniques that enhance crew health and physiological performance preflight, inflight, during reentry, immediately postflight, and between flights. Cumulative effects from exposure to multiple simulations of spaceflight are evaluated, as well as minimal intervals necessary for safe recovery between flights. Evaluations were made of methods to counteract deconditioning, such as exercise rehabilitation, drugs, and use of the inflatable G-suit as added protection against orthostatic intolerance during reentry of the Space Shuttle.

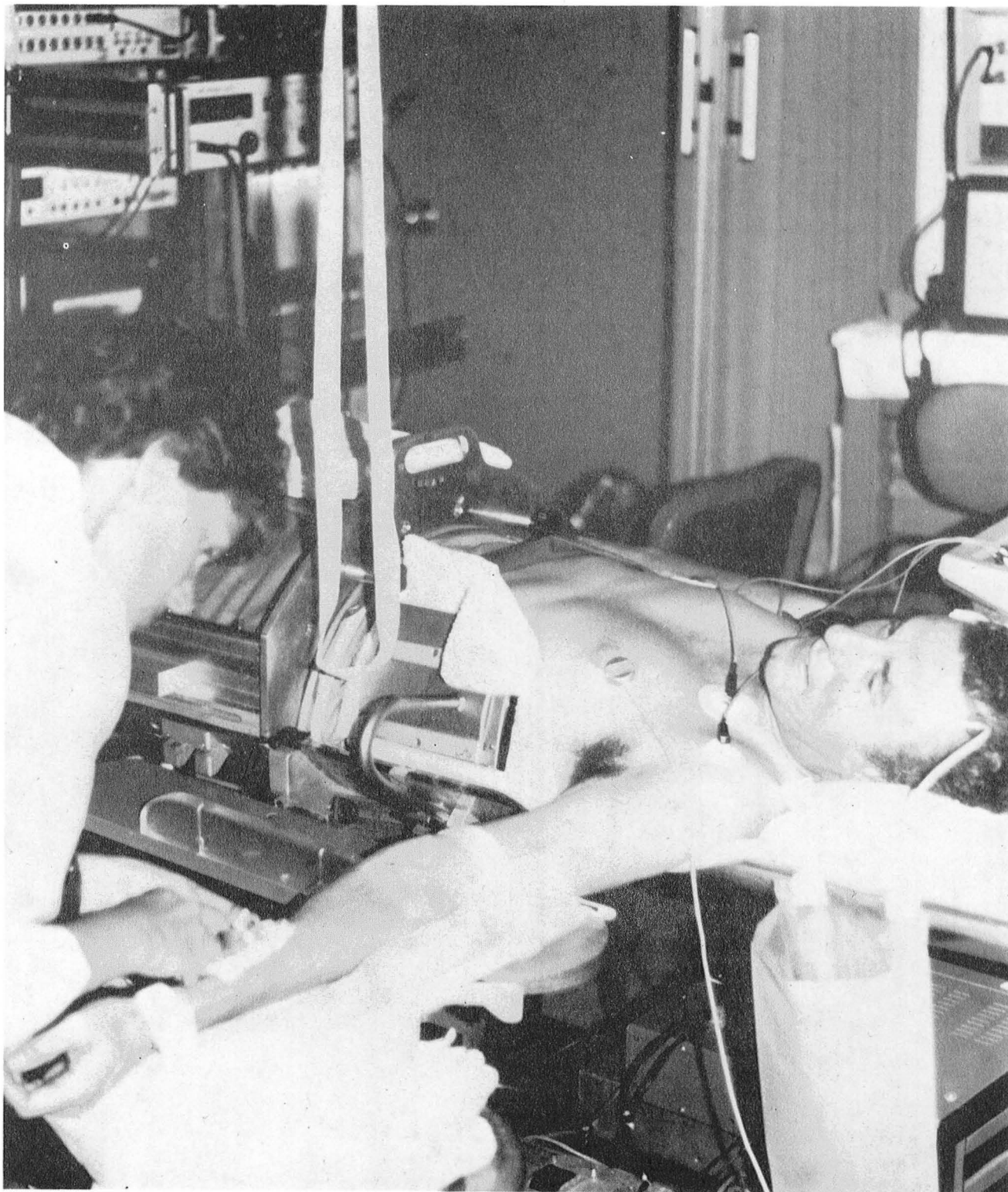


Fig. 2. Subject undergoing lower body negative pressure (LBNP) has blood sample drawn for assessment of plasma renin, catecholamines, arginine vasopressin and aldosterone after propranolol injection, a possible countermeasure for orthostatic intolerance following weightless flight. (Harrison and Kates 199-10-32-09)

PHARMACOLOGIC COUNTERMEASURES FOR CARDIOVASCULAR DECONDITIONING DURING SHUTTLE FLIGHT 199-10-32-09

D.C. Harrison and R.E. Kates, Stanford University, School of Medicine
D.J. Goldwater, Ames Technical Monitor

An extensive study evaluated potential drug countermeasures: atropine, phenylephrine, and propranolol. In some cases, preliminary analysis revealed a differential drug effect depending on the subject's level of aerobic conditioning. All drugs were tested against placebo injection in single blind fashion. Phenylephrine significantly prolonged tolerance (+35%) after Shuttle flight simulation. Atropine tended to prolong lower body negative pressure (LBNP) tolerance to a greater degree after bedrest. After bedrest, the same dose of atropine produced a larger resting increase in heart rate over the placebo. This result suggested either lower vagal tone or greater resting beta-adrenergic sympathetic tone after weightlessness simulation. Because the response of the resting heart rate to propranolol (compared to placebo) was no different after bedrest, lower vagal tone at rest may be responsible for the increased effect of atropine.

During LBNP stress, sympathetic tone was greater after bedrest than pre-bedrest. Further, the same dose of propranolol produced less of a heart rate decrease during peak LBNP levels compared to the placebo (Fig. 2). Greater sympathetic tone may explain propranolol's less deleterious effect on LBNP tolerance after bedrest compared to pre-bedrest. This data suggested that phenylephrine and atropine may be useful during Shuttle reentry and post-flight periods; however a careful dose response study must be conducted to further evaluate propranolol.

This laboratory also perfected a chromatographic assay for epinephrine and norepinephrine microdeterminations with a lower limit of sensitivity of 50 pg/ml. Investigators started assays on dozens of blood samples from this study that were taken during each level of LBNP so that the drug effects of orthostatic tolerance can be assessed.

Publications: none

ATHLETIC CONDITIONING AND REPEATED WEIGHTLESSNESS EXPOSURES 199-10-32-17

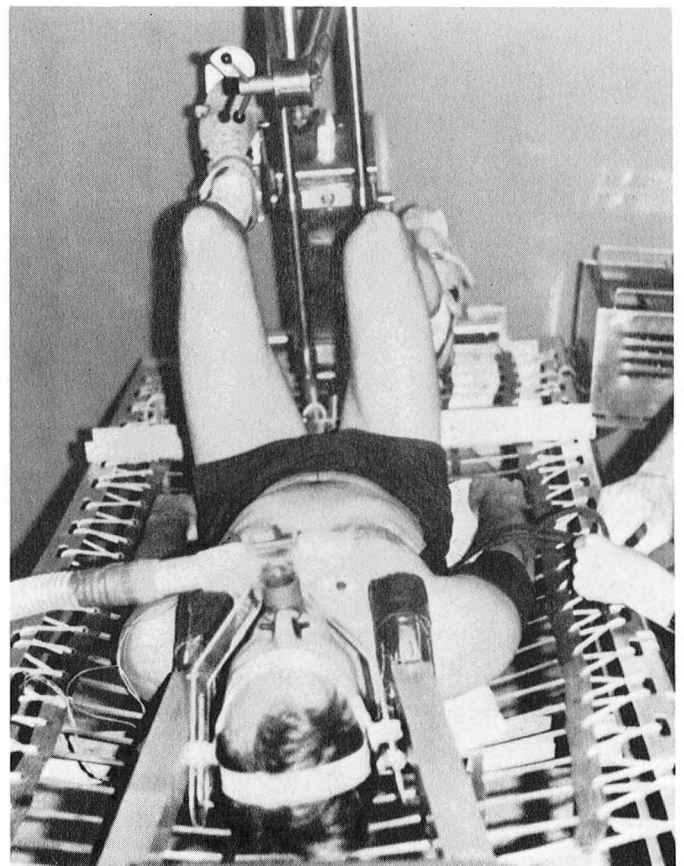
D.J. Goldwater, Ames Research Center, Biomedical Research Division

The first study in this series was conducted with sedentary and aerobically-conditioned men aged 35 to 50 years (Figs. 3, 4, and 5). Results indicate that, prior to bedrest, maximum oxygen consumption (VO_{2max}), plasma volume and age were not predictors of orthostatic tolerance tested by lower body negative pressure (LBNP). Surprisingly, high pre-bedrest tolerance to LBNP was associated with greater fluid accumulation in the mid-thigh and greater vascular compliance in the leg during LBNP. However, compared to subjects with low pre-bedrest tolerance, high tolerance subjects were able to compensate with significantly greater heart rates and higher mean arterial pressures. Pre-bedrest VO_{2max} correlated inversely with +3 Gz acceleration tolerance prior to bedrest.



Fig. 3. Subject begins maximal Bruce treadmill protocol to determine maximum oxygen consumption (VO_{2max}) after simulation of a Space Shuttle flight. (Goldwater 199-10-32-17)

Fig. 4. Subject undergoes maximal supine ergometry after bedrest. The supine position allows determination of 'weightless' or 'inflight' aerobic capacity (VO_{2max}) without the effects² of gravity on upright posture. (Goldwater 199-10-32-17)



Cycle ergometer VO_2max decreased by 8.7% after an initial bedrest period and by 5.2% after a second bedrest period, but returned to pre-bedrest values after 14 days of recovery. Similarly, anaerobic work threshold and plasma volume decreased significantly during each simulated ten-day Shuttle flight, but recovered after 14 days. Some recovery may be attributed to the vigorous LBNP and acceleration testing conducted for several days prior to the exercise tests.

Body fat, body weight, plasma viscosity, total cholesterol, HDL cholesterol, triglycerides, and glucose intolerance successively increased with each bedrest period and did not recover after 14 days. These results suggested that exercise capacity may return to normal after two Shuttle flights separated by only 14 days; however factors frequently associated with coronary risk require a longer recovery period between flights or at least a vigorous exercise program during the two-week interval.

Publications: (1) DeBusk, R., V. Convertino, J. Hung, and D. Goldwater. 1983. "Exercise conditioning in middle-aged men after ten days of bedrest." CIRCULATION 68: 245-250. (2) Hung, J., D. Goldwater, V. Convertino, J. McKillop, M. Goris, and R. DeBusk. 1983. "Mechanisms for decreased exercise capacity following bedrest in normal middle-aged men." AMERICAN JOURNAL OF CARDIOLOGY 51: 344-348.

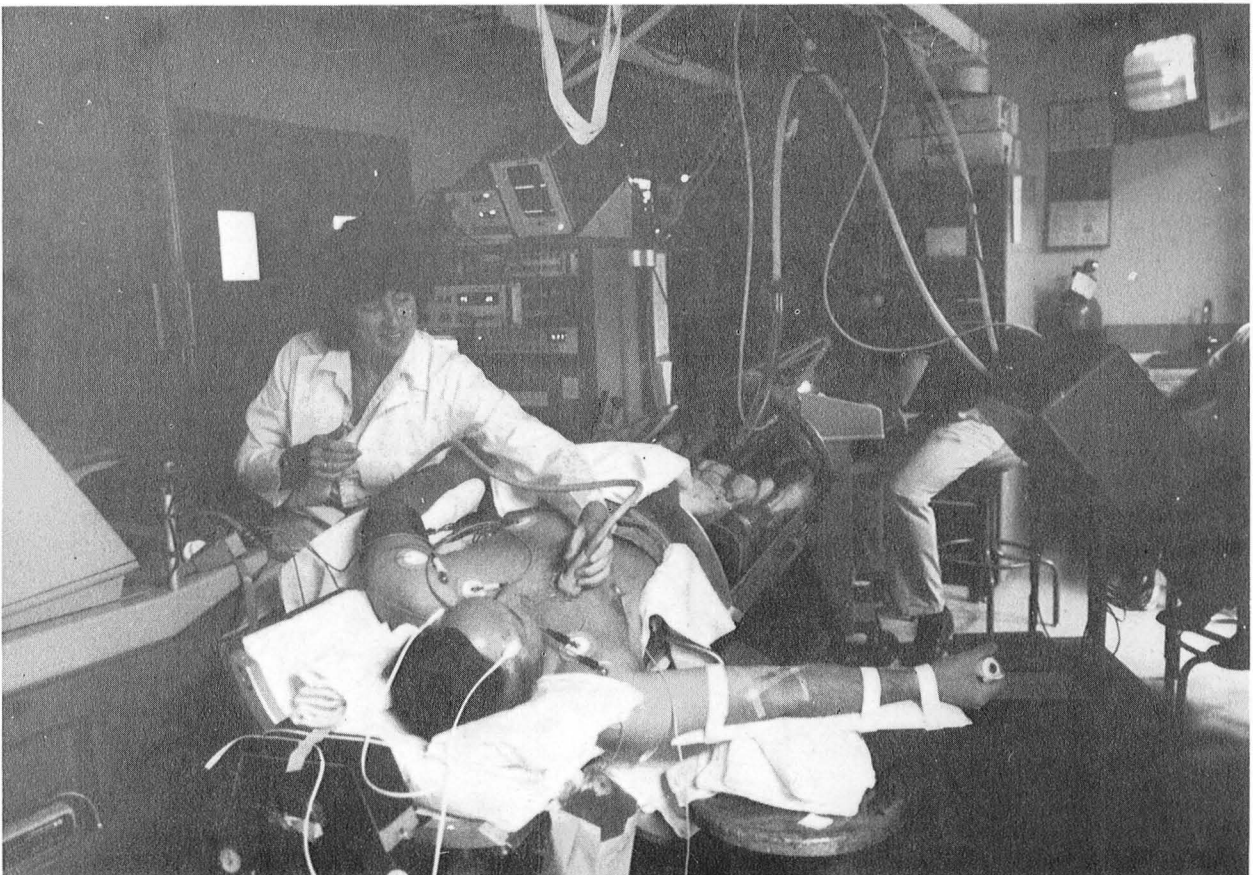


Fig. 5. Middle-aged man undergoing echocardiography during lower body negative pressure (LBNP) at -100 mmHg (below atmospheric). He is rotated 30° to the left to allow better visualization of the heart. (Goldwater 199-10-32-17)

SPACE ADAPTATION SYNDROME

SPACE ADAPTATION SYNDROME

AMES RTOP 199-10-62

H.J. Finger, manager

P.S. Cowings, principal investigator

While individuals on the Skylab flights in the mid-1970s experienced different susceptibilities to the nausea of space motion sickness, they adapted to this effect of weightlessness within three to five days after launch. Because current shuttle missions are generally of this duration, it is desirable to ameliorate space motion sickness during the susceptible period to maximize astronaut performance capability. Pioneer researchers in biofeedback over the past 20 years and a team of NASA scientists developed the technique of Autogenic Feedback Training (AFT), allowing subjects to successfully control their own motion sickness symptoms.

Functionally, as an individual thinks of any bodily movement, corresponding electrical activity can be measured in the nerves and muscles, even if the person does not move at all. Obviously, the brain plays a large role in controlling bodily functions. Using this basic physiological fact, a precise training regimen was experimentally developed over the past decade at Ames Research Center. Using miniature electronic monitoring equipment, subjects easily learned to monitor and control some of their own vital signs and other physiological processes, such as heart rate, muscle tension, and motion sickness symptoms, using AFT. Following the training, individuals could use this ability without further need of bioelectric monitoring devices. Such self-suggestion techniques were used by the U.S. Air Force in a study to return to flight status 80% of pilots grounded for motion sickness. As a result, the USAF requested AFT for their astronauts in preparation for future Space Shuttle flights.

Using AFT in the laboratory: 1) subjects withstood Coriolis acceleration significantly longer and at higher velocities than control subjects; 2) subjects had equal success in controlling symptoms, regardless of their gender or their past susceptibility to motion sickness; and 3) subjects could be trained to control motion sickness under one type of stimulation (e.g., Coriolis acceleration), yet would be immune to motion sickness under other stimuli (e.g., visual stimulation or linear acceleration). No other motion sickness countermeasure, including drugs, has been shown to remedy several different stressful situations. Careful experimentation also yielded information on the types of schedules and electronic feedback displays that produce the greatest amount of learned self-control in a minimal amount of time. Some subjects, who received only six hours of AFT, could control symptoms up to two years following training.

The scientific validation of AFT during spaceflight is scheduled to begin on Spacelab 3 with five astronauts: three trained and two untrained controls. The astronauts will monitor autonomic nervous activity to control their symptoms and to provide an objective measure of the success of AFT during spaceflight. With a good return on flight data, a minimum participation of 16 astronauts (eight trained, eight untrained) is required during flight tests to obtain a sufficient database for scientific statistical analysis.

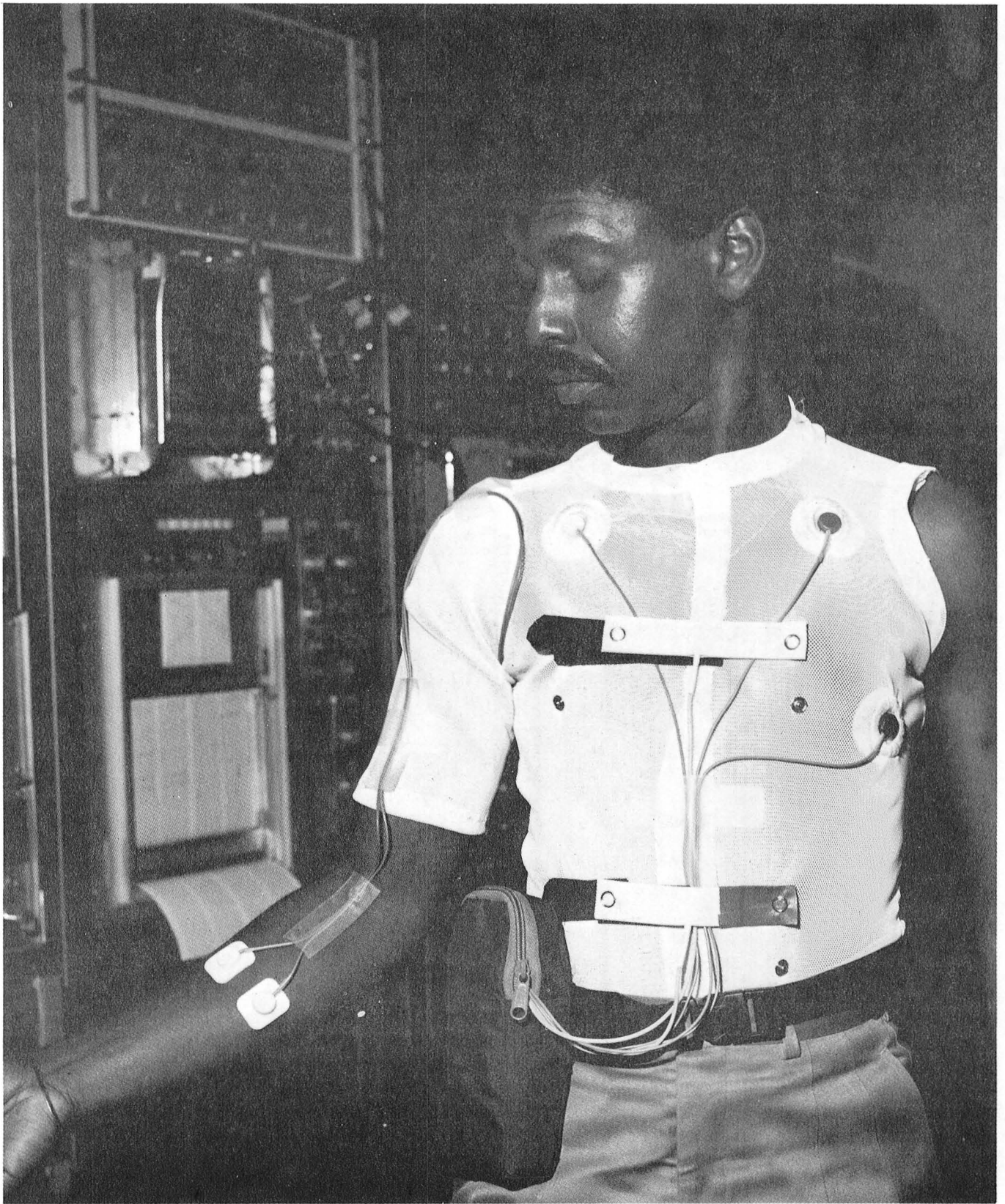


Fig. 6. Prototype ambulatory monitoring garment and transducer configuration. (Cowings 199-10-62-01)

SPACELAB 3 AFT FLIGHT EXPERIMENT 199-10-62-01

Scientific Collaborators

P.S. Cowings, Ames Research Center, Biomedical Research Division
J. Kamiya and W.B. Toscano, University of California Medical Center,
Langley Porter Neuropsychiatric Institute
N.E. Miller, Rockefeller University, Department of Psychology
J.C. Sharp, Ames Research Center, Deputy Director of Life Sciences

Engineering Design

H.J. Finger, Ames Research Center, Systems Engineering Division
L.E. Edsinger, Ames Research Center, Systems Engineering Division

Prime Contractor

SRI International, Menlo Park, CA

Prototype transducers and amplifiers for monitoring physiological activity were developed and tested on 20 men and women during baseline, motion sickness-inducing, and ambulatory conditions. Optimal transducer types and locations were determined (Fig. 6). Transducers and cables were mounted on garments worn by ambulatory subjects. Different types of garments were designed and fabricated for these tests to determine functionality, ease of donning and doffing, and comfort. Information gained on amplifier and transducer configurations will be incorporated into the final design of flight hardware. Signal acquisition software was written for a data recorder to assess data dropout during ambulatory sessions. These signal processing algorithms will be included in the software package designed for the cassette tape playback unit (flight data recording system).

Instructional materials and procedures were developed for training crewmembers to self-diagnose malaise in flight. Overt signs of motion sickness (e.g., degrees of facial pallor and sweating, etc.) were videotaped from human subjects during zero gravity parabolas in the Lear jet. Preliminary tests indicated that video tapes greatly aided training subjects to recognize and score their own motion sickness symptoms using a standardized diagnostic scale.

Publications: none

BIOMEDICAL RESEARCH

THE BIOMEDICAL RESEARCH PROGRAM IN NASA

The Biomedical Research Program is designed to investigate the major physiological and psychological problems encountered by man in space and to develop solutions. The program strives for a better definition of each problem, an understanding of underlying mechanisms and ultimately a means of prevention. The program deals with the specific physiological problems that have either been encountered in previous US and USSR manned spaceflight or which are anticipated to occur as spaceflights become longer, traverse more distant trajectories or are otherwise different from previous missions. Currently, emphasis is placed on motion sickness and cardiovascular problems because of their potentially adverse impact on short duration Space Shuttle missions. Musculoskeletal research is undertaken because of the very important fundamental knowledge that must be acquired before countermeasures to the effects of repetitive or long-term flight can be devised. Increased concern for the radiation hazard has resulted in more attention being focused on the biological effects of high energy, high mass number particulate radiation and upon radiation protection. Major future thrusts must deal with the psychological challenges of spaceflight and in particular with the need to enhance human performance in all categories of inflight activity. Although the foregoing research is, by definition, ground based, it is important to note that through it are developed hypotheses that must ultimately be tested in space. The program is intimately related to the ongoing series of inflight experiments on the Shuttle and Spacelab.

(From NASA Space Science and Applications Notice, October 25, 1982)

Paul C. Rambaut
Program Manager

CARDIOVASCULAR DECONDITIONING

Official Space Shuttle flight summaries identified effects on the cardiovascular system as a major medical problem. Compared to preflight measures, left ventricular size decreased 10% to 50%. Cardiovascular deconditioning also manifested as increased heart rate and lowered blood pressure responses to orthostatic tests during and after all manned spaceflights to date, despite the use of countermeasures. Postflight tests of deconditioning revealed a 10% to 50% loss of exercise capacity. Tolerance decreased similarly to lower body negative pressure (LBNP) tests, which simulate the effect of standing erect by reducing air pressure from the waist down, thus forcing blood flow toward the legs. During the first week postflight, astronauts' heart rates rose to twice their preflight levels during LBNP tests. Tolerance to posture (tilt table) tests, where astronauts were tilted vertically from a horizontal position, also decreased 10% to 50%.

Detailed physiological effects during reentry of the Shuttle remain unknown. Sustained head-to-foot (+Gz) acceleration experienced by astronauts sitting erect lasts 18 to 20 minutes, and is unique to the Shuttle.

Losses of intravascular volume, changes in control by the central and/or peripheral nervous system, and losses in ventricular muscle mass influenced cardiovascular deconditioning, as deduced from both studies on Earth and results from flight. Following hypokinesia on Earth, rhesus monkeys (Macaca mulatta) lost heart muscle and registered reduced orthostatic tolerance (susceptibility to fainting). Involvement of the nervous system in control of cardiovascular functions appeared to cause a 50% reduction in effectiveness of vasoactive drugs in the immobilized monkey. Astronauts and cosmonauts were not studied in this regard.

In addition to studies of horizontal immobilization on the rhesus monkey, immersion of animals and humans up to the neck in a bath of warm water also simulated some of the effects of weightlessness. Investigators used a tilt table following immersion to test for orthostatic tolerance as a sign of cardiovascular deconditioning.

Because actual results from flight are the final validation of hypotheses from ground experiments, miniature, implantable bioinstruments were developed and tested to record blood flow and pressure in a small rhesus monkey in preparation for flight on a five-day Cosmos mission. This engineering test flight, the first in the Cosmos series with a nonhuman primate, was the fourth unmanned flight of animals in a cooperative program with Soviet scientists (see pg. 147).

H. Sandler, Ames Research Center, Biomedical Research Division
B.A. Benjamin, National Research Council Associate
F. King, Emory University, Yerkes Primate Research Center, Atlanta, GA

Simulation of weightlessness in animals, as well as in humans, is used in developing countermeasures to cardiovascular changes observed during spaceflight. Initial bodily changes to weightlessness include a lower heart rate with an enlarging of the heart to handle the increased volume of blood. The initial effects of return to +1G are the opposite. Headward shifts in blood volume during weightlessness may also influence secretion of antidiuretic hormone (ADH) which, in turn, controls blood pressure and volume.

Ground-based studies, simulating the effects of spaceflight, showed cardiovascular changes in the small rhesus monkey (*Macaca mulatta*) similar to changes observed in humans from bedrest and water immersion. ADH levels decreased to reduce the headward increase of blood in both monkeys and humans. In a study using eight monkeys, the cardiovascular response of awake animals most closely approximated the response in humans, as compared to animals tranquilized with ketamine or anesthetized with pentobarbital.

Preceding a joint US-USSR engineering test flight that orbited two nonhuman primates, ground simulations documented the daily changes in blood pressure, cardiac output, heart rate, and rectal temperature for one to two-week periods. A surgically-implanted cuff measured blood pressure and flow in the carotid artery. Preparations were made to compare laboratory data to flight data, which will provide the first accurate measurements in the primate of blood flow to the head during launch, orbit, and landing.

At Stanford University Medical Center, heart and heart-lung transplant patients were studied to determine which nervous pathways signal the body to alter cardiovascular flow in response to change in body position. Results during a tilt experiment showed that the blood pressure, heart rate and ADH responses in the patients with completely denervated hearts was similar to normal control subjects with non-denervated hearts. When subjects were tilted head down from a horizontal position, the high pressure baroreceptors in the aortic arch apparently played a role in regulation of blood volume and blood pressure because the action of ADH was similar in both groups.

Publications: (1) Dickey, D.T., G.E. Billman, M.J. Keyl, D.A. Ken, L.C. Keil, H. Sandler, and H.L. Stone. 1983. "Hormonal and renal responses to plasma volume expansion after horizontal restraint in the rhesus monkey." AEROSPACE MEDICAL ASSOCIATION PREPRINTS 100-101. (2) Lin, Y.C., E.L. Carlson, E.P. McCutcheon, and H. Sandler. 1983. "Cardiovascular functions during voluntary apnea in dogs." AMERICAN JOURNAL OF PHYSIOLOGY 245: R143-R150. (3) Sandler, H., 1982. "Cardiovascular responses to weightlessness and prolonged bedrest." in A Critical Review of the U.S. and International Research on Effects of Bedrest on Major Body Systems. Nicogossian, A.E., and C.S. Lewis, eds. Washington, D.C.: NASA pp. 3-80. (4) Sandler, H. 1983. "Are There Limits To Man's Long-term Presence in Space?" SAE Technical Paper Series 831132. Available from: Society of Automotive Engineers, 400 Commonwealth Drive, Warrendale, PA 15096. (5)

Sandler, H., and T.F. Budinger. 1983. "Recent advances in physiological monitoring: Opening remarks." *PHYSIOLOGIST* 26(1) 29-30. (6) Sandler, H., P. Webb, J. Annis, N. Pace, B.W. Grunbaum, D. Dolkas, and B. Newsom. 1983. "Evaluation of a reverse gradient garment for prevention of bed-rest deconditioning." *AVIATION, SPACE AND ENVIRONMENTAL MEDICINE* 54(3): 191-201.

BIOTELEMETRY SYSTEMS FOR CARDIOVASCULAR FLIGHT EXPERIMENTS 199-20-12-07

J.W. Hines, U.S. Air Force detailee at Ames Research Center
H. Sandler, Ames Technical Monitor

Weight, space, and electric power limitations aboard today's space vehicles require the use of small rhesus and squirrel monkeys as animals best simulating human cardiovascular responses. Instrumentation packages are readily available for use in large, but not small, animals. Work continued to redesign and miniaturize available systems for use in animals as small as 3 kg. A trailer was equipped for making long-term cardiovascular measurements in primates, as well as for in vivo testing of hardware (programmed circuitry) and telemetry systems.

A combined pressure and flow (CPF) cuff, fitting around the carotid artery, accurately measured blood pressure and flow to the head (Fig.7). These

REPRESENTATIVE WAVEFORMS FROM CPF CUFF

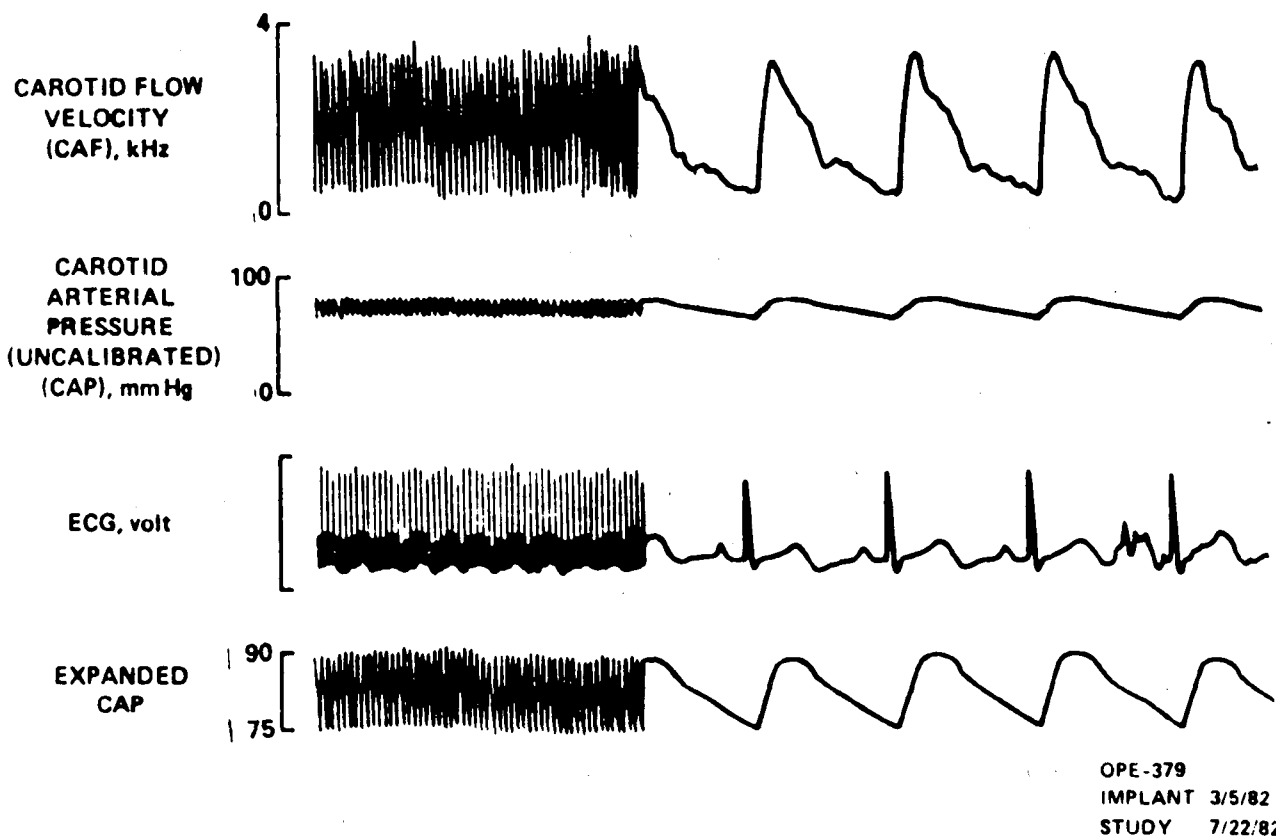


Fig. 7. Blood flow, carotid arterial pressure (CAP), and ECG signals recorded from the combined pressure and flow (CPF) cuff developed for implantation in a rhesus monkey for Cosmos 1514. (Hines 199-20-12-07)

CPF pressure-sensing transducers passed a two-month accuracy test prior to implantation in a small rhesus (Macaca mulatta) for the test flight of a joint US-USSR unmanned Cosmos biosatellite. A test of data transfer from Soviet to NASA tape recorders was also successful.

Publications: Sandler, H., and J.D. Meindl. 1983. "Telemetry methods: Animal and man." *PHYSIOLOGIST* 26(1): 47-50.

CENTRAL AND PERIPHERAL MECHANISMS MODULATING CARDIOVASCULAR DECONDITIONING IN UNANESTHETIZED PRIMATES 199-20-12-11

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H. Sandler, Ames Technical Monitor

Under simulated flight conditions, investigators studied the role of baroreceptors (in the carotid artery), affecting changes in ADH production by the pituitary to control blood pressure. Rhesus monkeys (Macaca mulatta), horizontally positioned, showed signs similar to findings from spaceflight in humans: decreased tolerance to +Gz acceleration typical during Space Shuttle reentry, decreased plasma volume and red cell mass, and decreased orthostatic tolerance (the ability to function normally without blackout or greyout after a change in posture, such as from horizontal to vertical). After one to four weeks of restraint, the animals showed a reduced response to vasoactive drugs, which constrict blood vessels to maintain pressure. The baroreceptor control of heart rate also decreased in sensitivity during this period. This study was the first time that the central nervous system was shown to be affected in the process of cardiovascular deconditioning.

Studies of the monkey showed that, after seven or 14 days of hypokinesia, a 25% increase in blood volume activated the kidney's compensatory mechanism, which decreased circulating levels of ADH (Fig. 8) and aldosterone to reduce the body's fluid volume and blood pressure. Thus, both the renal system and endocrine system account for the changes associated with orthostatic intolerance.

Publications: (1) Billman, G.E., M.J. Keyl, D.T. Dickey, D.C. Kem, L.C. Keil, and H.L. Stone. 1983. "Hormonal and renal response to plasma volume expansion in the primate Macaca mulatta," *AMERICAN JOURNAL OF PHYSIOLOGY* 244: H201-H205. (2) Dickey, D.T., G.E. Billman, M.J. Keyl, D.A. Kem, L.C. Keil, H. Sandler, and H.L. Stone. 1983. "Hormonal and renal responses to plasma volume expansion after horizontal restraint in the rhesus monkey." *AEROSPACE MEDICAL ASSOCIATION PREPRINTS* 100-101.

EFFECTS OF SIMULATED WEIGHTLESSNESS ON PERIPHERAL AND CARDIAC ADRENERGIC RECEPTORS 199-20-12-15

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For the first time changes in blood flow to various organs was studied systematically in the rhesus monkey (Macaca mulatta) under ground-based

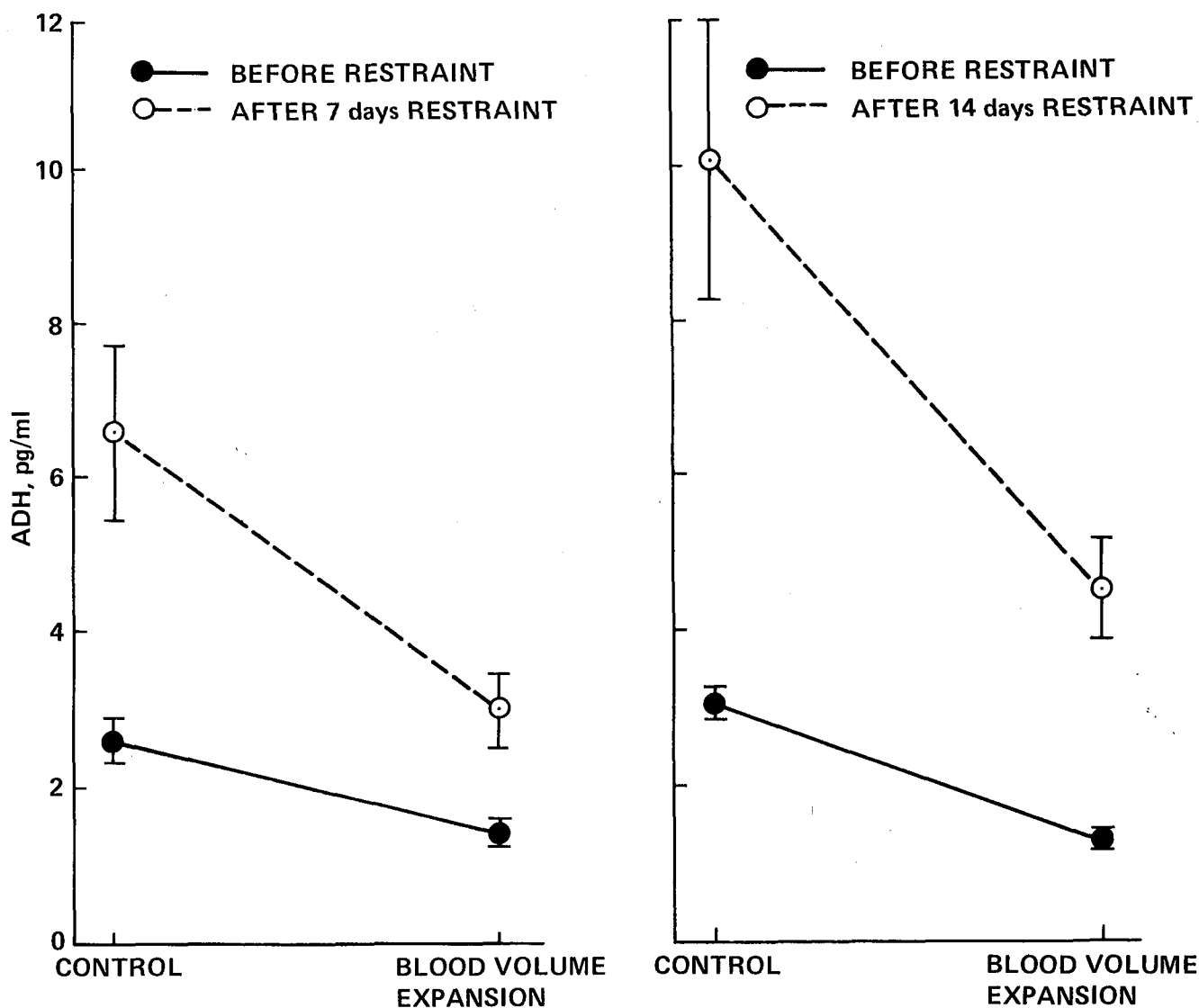


Fig. 8. The longer the exposure to simulated spaceflight, the more severe the drop in plasma levels of antidiuretic hormone (ADH) during volume loading. ADH secretion helps the body maintain blood pressure by holding water. (Stone 199-20-12-11)

conditions known to produce physiological changes similar to those that occur during spaceflight. Of particular interest were changes in blood flow to the brain, liver, kidney, gut, skeletal muscle, and especially the heart, because myocardial degeneration in primates followed prolonged periods of immobilization, suggesting a risk in humans from prolonged periods of weightlessness.

Monkeys were injected with radioactively-labeled microspheres to determine blood flow during water immersion and exposure to five different body positions: seated upright ($+90^\circ$), head up ($+45^\circ$), horizontal (0°), and head down (-6° and -25°). Flow to the left ventricle averaged 3.5l

ml/min/g under most conditions, but increased to 5.06 ml/min/g during -25° tilt, and 8.47 ml/min/g during water immersion. Similar results were noted for the right ventricle. The two significant increases in coronary blood flow most likely resulted from a larger volume of venous blood returning to the heart, and from a change in curvature of the ventricle walls, increasing their radius. Presumably, these changes increased myocardial oxygen demand with a concomitant demand for increased coronary blood flow.

No significant differences during different body positions were observed in the kidneys, spleen, or skeletal muscle, but the data were limited. Cerebral spinal fluid (CSF) pressure increased in the head-down positions. CSF pressure (approx. 6 mmHg) during water immersion was most similar to pressure recorded at -6° . Approximately 10 mmHg, the highest CSF pressure, occurred during -25° head-down tilt.

Publications: none

CONTROL OF NATRIURESIS UNDER CONDITIONS OF SIMULATED AND TRUE WEIGHTLESSNESS 199-20-12-16

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H. Sandler, Ames Technical Monitor

Cardiovascular, renal, and hormonal responses were studied in the conscious rhesus monkey (Macaca mulatta) during water immersion. Anesthetized and tranquilized monkeys were also studied to determine the effects of certain drugs on the immersion response. Results from the conscious animals showed that water immersion caused a diuresis, natriuresis (increased sodium excretion), and reduced ADH response similar to immersion in humans (Fig. 9). Anesthetized and tranquilized animals showed changes in their renal and hormonal response that differed significantly from human results. Atrial tissue was obtained and stored until a procedure is perfected to isolate an atrial natriuretic factor, which was experimentally observed by the Canadian researcher, de Bold (Proceedings of the Society for Experimental Biology and Medicine 170: 133-138, 1982). (This task was successfully completed and terminated.)

Publications: Bricker, N.S., and G.M. Danovitch. 1983. "Extracellular fluid volume regulation: On the evidence for a biologic control system," in The Kidney in Liver Disease, 2nd Edition. Epstein, M., ed. New York: Elsevier Biomedical. pp. 13-21.

MECHANISMS OF CIRCULATORY REGULATION WITH VOLUME LOADING AND DEPLETION IN CONSCIOUS ANIMALS 199-20-12-20

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Expansion, or loading, of plasma volume was hypothesized to occur in the

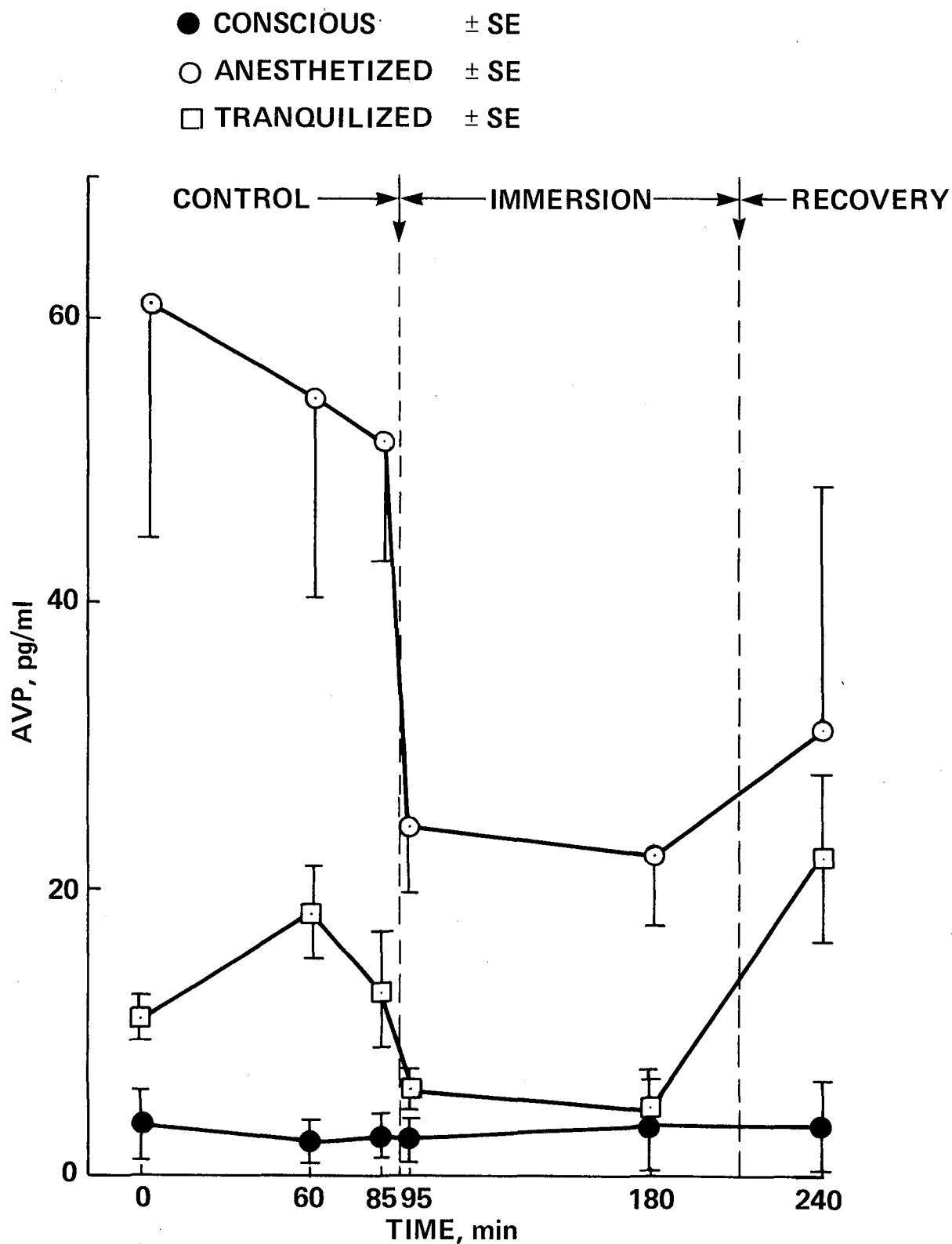


Fig. 9. During water immersion, results from the conscious rhesus (shown above) and humans revealed similar plasma levels of arginine vasopressin (AVP), also known as the antidiuretic hormone (ADH). (Bricker 199-20-12-16)

upper body during the early period of weightlessness in space, and during head-down tilt and lower body positive pressure (LBPP) tests on Earth. Volume loading was stimulated in the unanesthetized baboon (Papio anubis), whose larger size permitted instrumentation with existing transducers. The diuresis and natriuresis accompanying volume expansion was associated with increased renal blood flow and decreased renal vascular resistance. These changes did not occur in conscious animals. Studies of conscious dogs also demonstrated that cardiopulmonary reflexes did stimulate afferents of the vagus nerve to the brain, helping to mediate water excretion. But, cardiopulmonary reflexes neither mediated dilation of the renal vessels, nor enhanced sodium excretion in acute volume loading.

Publications: Zimpfer, M., W.T. Manders, A.C. Barger, and S.F. Vatner. 1983. "Pentobarbital alters compensatory neural and humoral mechanisms in response to hemorrhage." AMERICAN JOURNAL OF PHYSIOLOGY 243: H713-H721.

BASIC MECHANISMS OF SPACE MOTION SICKNESS

The limited room for movement, including head movement, by astronauts in the first generation space capsules may explain why space sickness was uncommon during the first decade of spaceflight. Since then nearly half of all space travelers experienced space motion sickness during the initial three to five days of weightlessness. During this period, half the duration of a typical Shuttle mission, malaise, disorientation, nausea, or vomiting prevented astronauts from operating at optimal efficiency.

Investigators conducting basic research at LR study the neural connections and biochemistry of the vestibular system (the organs of the inner ear), which supplies the sense of balance and orientation for all higher animals, including amphibians, birds, fishes, and mammals. The vestibular end organs of the inner ear sense changes in speed and direction during head movements. One part of the vestibular organs, the otolith organs, sense linear acceleration and gravity. The semicircular canals of the inner ear sense angular acceleration, such as rotating the head. Unlike the otolith organs, the semicircular canals do not depend on gravity, although recent evidence suggests that the neural output of the canals is influenced by output from the otoliths.

Humans participated in behavioral tests, involving linear acceleration (see pg. 52), preceding joint flight experiments by NASA and the European Space Agency (ESA) on Shuttle-Spacelab 1. Animals were used in behavioral, neuroanatomical, and neurochemical experiments. Using fragile microelectrodes and chemical stains, neuroanatomical researchers traced previously unknown pathways between various vestibular end organs and the brain. Other LR researchers suggested that a neurochemical factor may trigger motion sickness because symptoms were prevented by blocking the flow of cerebrospinal fluid to a vomiting trigger zone in the brain.

In space the brain must adapt to weightlessness-induced changes in the function of the vestibular system by greater reliance on cues from other senses, such as the eyes and neck muscles. The brain can also be trained to adapt quickly to changes in the sensory environment of the astronaut, using the self-control technique of Autogenic Feedback Training (AFT) developed for aerospace use over the past decade at Ames Research Center. A test of the usefulness of AFT as a treatment for space sickness is scheduled for Shuttle Spacelab 3 (see pgs. 27-29).

NASA's establishment of the Vestibular Research Facility (VRF) at Ames Research Center will provide investigators with specialized equipment and controlled experimental conditions to record eye movements and electrophysiological signals in a variety of species under many different conditions of visual and vestibular stimulation. NASA will provide engineering support and scientific coordination through a VRF Science Director, and will provide access for qualified investigators from the

scientific community to conduct vestibular experiments. Experience with the ground-based VRF will aid in the design of critical spaceflight experiments to clarify the role of gravity in vestibular function.

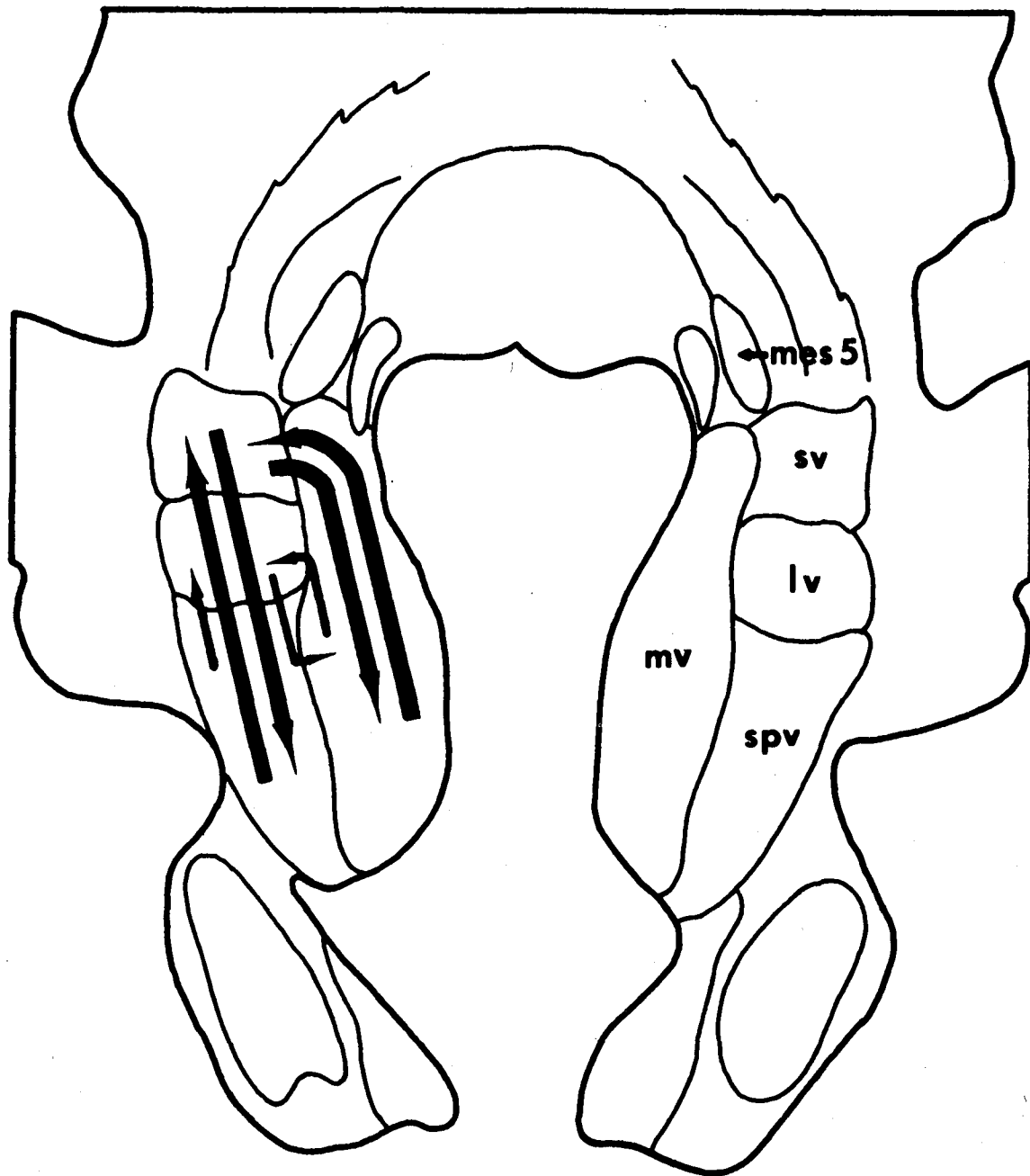


Fig. 10. In the brain stem of the rat, reciprocal internuclear connections link various vestibular nuclei (the four cellular masses on the floor of the fourth ventricle where the branches of the vestibular nerve terminate). The lateral vestibular (lv) nucleus and the medial vestibular (mv) nucleus mutually interconnect (small arrows). However, the lv does not reciprocate the input from the spinal vestibular (spv) nucleus, as indicated by the single small arrow, nor does the lv connect with the superior vestibular (sv) nucleus. Major reciprocal connections (bold arrows) exist among the superior, lateral and spinal nuclei, and between the medial and superior nuclei. (Mehler 199-20-22-03)

THE ANATOMY AND PHYSIOLOGY OF THE VESTIBULAR SYSTEM 199-20-22-03

W.R. Mehler, Ames Research Center, Biomedical Research Division

The end point to the vertigo and malaise of space sickness and other types of motion sickness, emesis is thought to be induced by impulses transmitted from the inner ear via primary vestibular fibers to the brain's vestibulo-cerebellum, and then to the vomiting "center" of the brain. A complete model of the vomiting "center," or vomiting trigger zone (VTZ), must include both the afferent connections towards, and the efferent connections away from this center. Therefore, research centered chiefly on finding the missing neurological link between the vestibulo-cerebellum and the VTZ. The VTZ was originally located neurophysiologically in the parvicellular reticular formation (pcRF) of the brain stem's medulla oblongata and reported by Borison and Wang in the Journal of Neurophysiology in 1949.

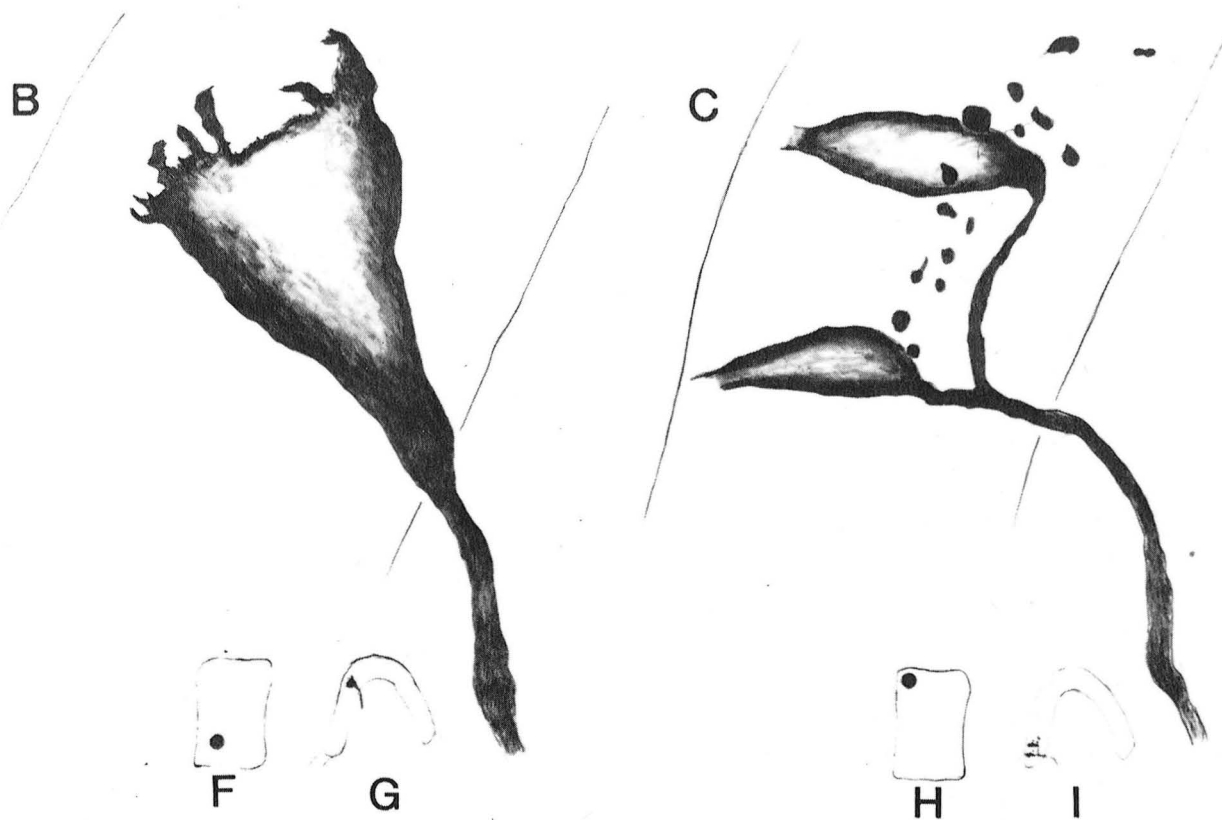
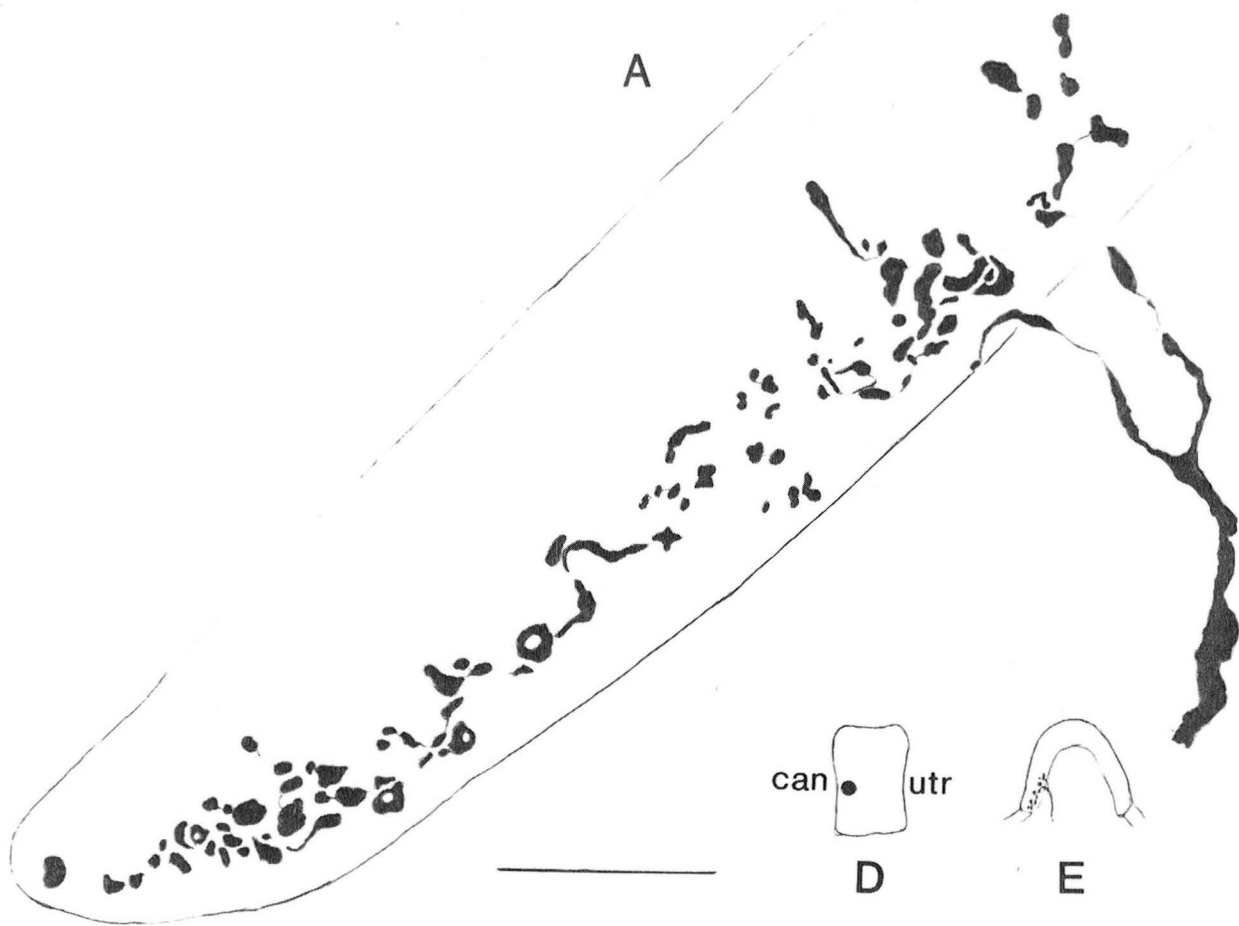
Researchers generated much new experimental and comparative data on the connectivity of the vestibular nerve, vestibular nuclei, and the brain stem's reticular formation. The pcRF, where electrical stimulation produced emesis, was further defined. Neuron staining with injections of horseradish peroxidase into the pcRF of 60 rats provided evidence of connections within the brain's vestibular complex (Fig. 10). The search continued for the definitive channel of afferent connection to the VTZ.

Publications: (1) Mehler, W.R. 1983. "Observations on the connectivity of the parvicellular reticular formation with respect to a vomiting center." BRAIN, BEHAVIOR AND EVOLUTION 23: 64-80. (2) Rubertone, J.A., W.R. Mehler, and G.E. Cox. 1983. "The intrinsic organization of the vestibular complex: Evidence for internuclear connectivity." BRAIN RESEARCH 263: 137-141.

PHYSIOLOGY OF THE VESTIBULAR SYSTEM IN THE SQUIRREL MONKEY 199-20-22-04

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N.G. Daunton, Ames Technical Monitor

Studies continued on the response characteristics of vestibular nerve afferents in the chinchilla (Chinchilla laniger). (Afferent neurons transmit sensory inputs to the central nervous system (CNS), and vestibular efferents transmit responses from the CNS to the vestibular end organs.) Peripheral innervation patterns of vestibular nerve fibers were traced in the inner ear of the chinchilla using microelectrodes, and extracellular injections of the stain, horseradish peroxidase (HRP). HRP was also injected intracellularly to relate stained innervation patterns to afferent structures. Three structural patterns, connecting sensory hair cells to vestibular nerves, were identified, as shown in Figure 11: bud-shaped (A), calyceal or cup-shaped (B), and an intermediate pattern, dimorphic (C). These three patterns were associated with nerve fibers of different fiber diameters, different discharge properties, and different proportions and distributions of fiber types in the sensory surfaces of the semicircular canals and the otolith organs.



Work continued on an intracellular study of secondary vestibular neurons in the vestibular nuclei of squirrel monkeys (Saimiri sciureus). Neurons that may innervate the oculomotor nuclei were compared to other neurons projecting to the cerebellum; these two types of neurons differed both in the profiles of ipsilateral vestibular nerve inputs, which come from the same side of the body, and in their commissural inputs, which come from the opposite side of the body.

Publications: (1) Goldberg, J.M. and C. Fernandez. 1982. "Eye movements and vestibular-nerve responses produced in the squirrel monkey to externally applied galvanic currents." EXPERIMENTAL BRAIN RESEARCH 46: 393-402. (2) Paige, G.D. 1983. "Vestibuloocular reflex and its interactions with visual following mechanisms in the squirrel monkey. I. Response characteristics in normal animals." JOURNAL OF NEUROPHYSIOLOGY 49: 134-151. (3) Paige, G.D. 1983. "Vestibuloocular reflex and its interactions with visual following mechanisms in the squirrel monkey. II. Response characteristics and plasticity following unilateral inactivation of horizontal canal. JOURNAL OF NEUROPHYSIOLOGY 49: 152-168.

FUNCTIONAL SIGNIFICANCE OF SENSORY INTERACTIONS IN SELF MOTION PERCEPTION AND MOTION SICKNESS 199-20-22-05

N.G. Daunton, Ames Research Center, Biomedical Research Division

Visual stimulation of the squirrel monkey produced motion sickness similar to that resulting from actual passive rotation. A visual field, rotating at $150^{\circ}/\text{sec}$, proved just as effective for inducing emesis in squirrel monkeys (Saimiri sciureus) as actually rotating them in darkness. Further, visual stimulation at $60^{\circ}/\text{sec}$ was more effective than passive rotation of the animal in producing motion sickness. The most provocative stimulation occurred when both visual and vestibular cues were available during passive motion. When the squirrel monkey was on a platform, rotating at the same rate and in the same direction as a surrounding visual field of vertical stripes (an optokinetic drum), the monkey had no visual cues of the rotation and the majority of the animals became sick to the point of vomiting. However, when concordant visual-vestibular stimulation

Fig. 11. Terminal fields for three superior semicircular canal units in the chinchilla stained by intra-axonal injections of horseradish peroxidase (HRP) through recording microelectrodes. Both unit A, a bud-shaped fiber located in the base of the crista (E) on its canalicular side (D), and unit C, a dimorphic fiber located at the base of the crista (I) on its canalicular side (H), had regular discharge patterns. Units A and C also showed relatively small responses to galvanic currents delivered by way of the round window, and small responses (characterized by phase lags to angular velocity) during 2 Hz sinusoidal head rotations. In contrast, unit B, the cup-shaped fiber located near the apex of the crista (G) on its canalicular side (F), had an irregular discharge, large galvanic responses, and large responses with large phase leads during 2 Hz head rotations. (Goldberg 199-20-22-04)

was provided by rotating the platform within the stationary optokinetic drum, sickness rates were significantly less. This information supports the hypothesis that sickness rates should be higher when the visual and vestibular cues conflict and do not provide adequate information for effective control of eye, head and body movements.

In studies of the rat as a potential animal model for motion sickness research, the area postrema (known to be essential for motion-induced vomiting in species with an emetic reflex) was not required for motion-induced taste aversion or for suppression of drinking. While these measures were thought to be species-specific reflections of motion sickness in the rat, our data suggested that caution should be exercised in the use of such measures as analogs of motion-induced vomiting.

Publications: (1) Crampton, G.H., and N.G. Daunton. 1983. "Evidence for a motion sickness agent in cerebrospinal fluid." BRAIN, BEHAVIOR AND EVOLUTION 23: 36-41. (2) Crampton, G.H., and N.G. Daunton. 1983. "Systemic naloxone increases the incidence of motion sickness in the cat." PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR 19: 827-829. (3) Sutton, R.L. "The effect of area postrema lesions on development of motion-induced conditioned taste aversion in rats." San Jose, CA: San Jose State University, 1983. Master's Thesis.

HABITUATION TO NOVEL VISUAL-VESTIBULAR ENVIRONMENTS WITH PARTICULAR REFERENCE TO SPACEFLIGHT 199-20-22-09

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N.G. Daunton, Ames Technical Monitor

Space motion sickness may result from conflicting information provided by otolith organs and semicircular canals, vision and proprioception (feedback from muscles and joints). Motor outputs were studied that reflect visual-vestibular interactions (VVI) as a paradigm for the study of multisensory integration and of adaptation. Using our expanded linear motion capabilities, experiments were begun to study linear VVI. Experiments were performed in which human subjects null their perceived motion under the influence of differing visual fields. Measurements were made of ocular torsion, or counterrolling of the eye, to visual motion stimuli. (Ocular torsion is known to be produced by lateral, or left-right, head tilt; and is thought to be produced by stimulation of the otolith organs, which sense linear acceleration and gravity.) Responses reflecting the subject's interpretation of the visual and vestibular inputs were analyzed by Fourier analysis.

The dynamic response of ocular torsion (rotation of the eye) to changing linear acceleration was measured in subjects, who focused their gaze on a red light while wearing specially-marked contact lenses (Fig. 12). The approximate frequency response up to 1.0 Hz was demonstrated at a sampling rate of three per second. This simple linear model proved adequate to measure the relationship between ocular torsion and angular deviation of the specific force vector. To the extent that ocular torsion reflects visually-induced tilt, rather than causes it, ocular torsion could serve as

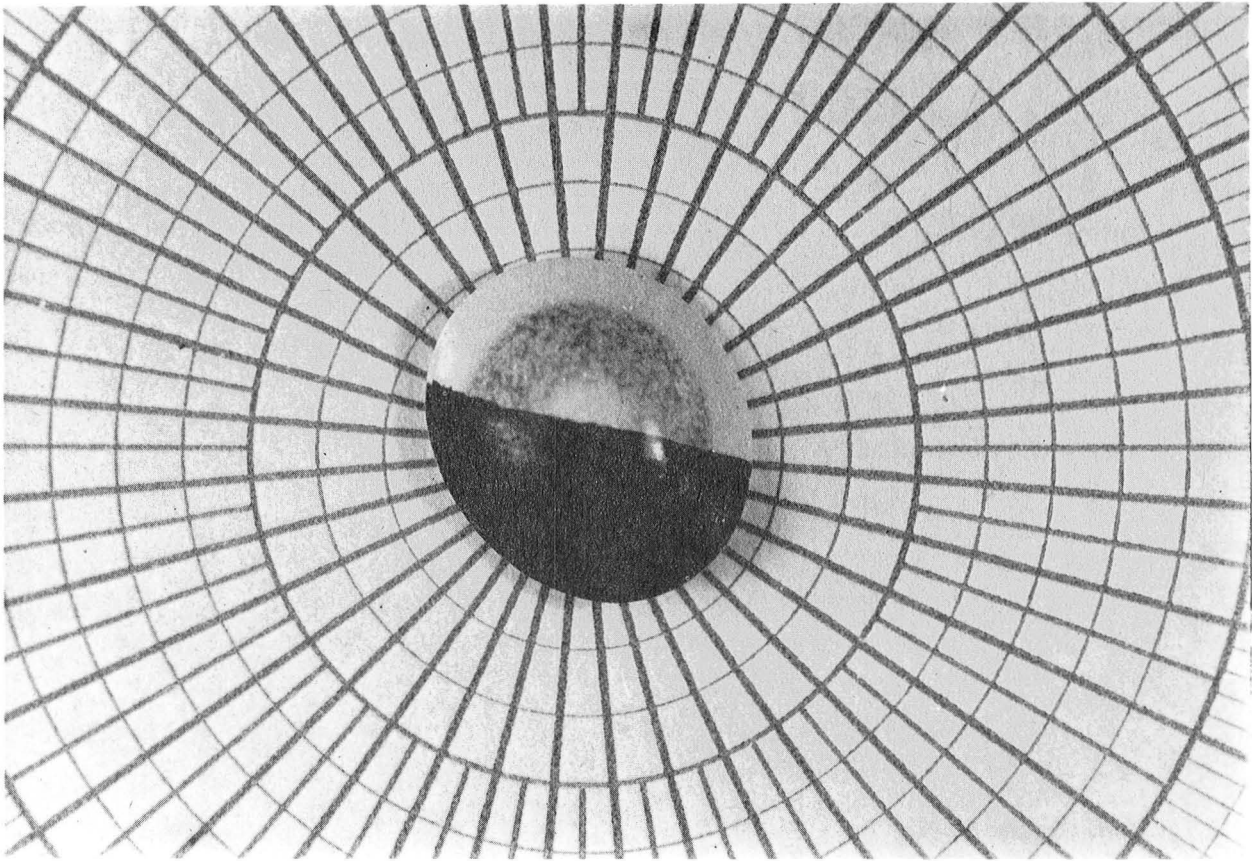


Fig. 12. Shown against a polar background, a half black, half white, soft contact lens was used as a border for measuring torsional movements as the eyes tracked a red light. Lenses were produced under a special process. Recordings were made with two phototransistors during rotation of the subjects around the roll axis, which primarily stimulated the vertical semicircular canals. (Young 199-20-22-09)

a convenient, objective measurement of VVI, and would not require voluntary, conscious participation by the subject. Experimental results to date indicated a very poor correlation between subjective indications of vection and ocular torsion, although they are clearly not independent. The simultaneous measurements of ocular torsion and vection were taken in the laboratory, during the zero-gravity portions of parabolic flights, and during 2 G phases of the parabolic flights. Results from these studies supported the visual-vestibular experiments on Shuttle-Spacelab 1 (STS-9).

Publications: (1) Lichtenberg, B.K., L.R. Young, and A.P. Arrott. 1982. "Human ocular counterrolling induced by varying linear accelerations." *EXPERIMENTAL BRAIN RESEARCH* 48: 127-136. (2) Oman, C.M. 1982. "A heuristic mathematical model for the dynamics of sensory conflict and motion sickness." *ACTA OTO-LARYNGOLOGICA* Supplement 392. 44p. (3) Young, L.R., T.A. Crites, and C.M. Oman. 1983. "Brief weightlessness and tactile cues influence visually induced roll." *ADVANCES IN OTO-RHINO-LARYNGOLOGY* 30: 230-234.

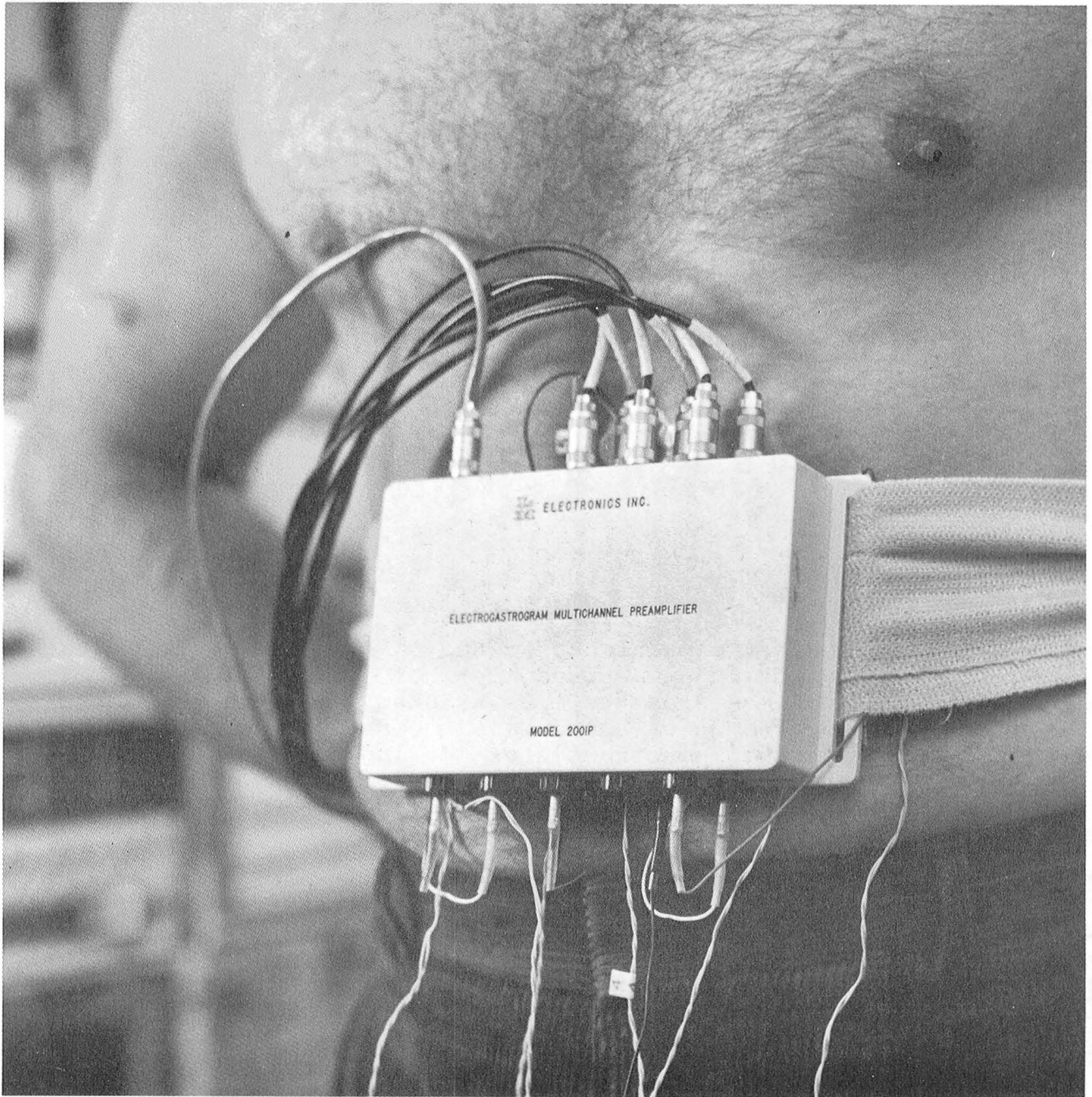


Fig. 13. A preamplifier was developed exclusively for laboratory experiments on Earth to establish baseline data of electrogastrograms (EGG) during motion sickness tests. Transducers were positioned under the preamplifier to monitor movements of stomach muscles. (Cowings 199-20-22-10)

PSYCHOPHYSIOLOGY OF MOTION SICKNESS 199-20-22-10

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The investigator obtained data of autonomic response patterns (stress profiles) of men and women aged 30 to 50 under multiple conditions that induce motion sickness. Adding these data to the existing data base will facilitate statistical analyses designed to determine the relationship of individual differences in stress profiles to age, sex, susceptibility, and type of motion stimulus. In another experiment, electrogastrogram (EGG) activity was monitored (Fig.13) continuously throughout Coriolis motion sickness tests of 20 men and women. All subjects showed a significant increase in EGG amplitude and slowing of frequency (<1 cpm) at the point of severe malaise. These findings suggest that non-invasive EGG measurement may be a reliable, objective indicator (i.e., autonomic concomitant) of subjectively reported nausea. Also software development was completed along with testing procedures for pilot studies that are necessary for investigating individual differences in cardiopulmonary function of subjects, who are susceptible in varying degrees to motion sickness.

Publications: none

HISTOCHEMICAL CHARACTERIZATION OF THE CNS EMETIC APPARATUS 199-20-22-11

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Research Center

W.R. Mehler, Ames Technical Monitor

A recent technique in functional neuroanatomy, the use of radioactive 2-deoxyglucose (2-DG), provided a pictorial representation of relative rates of glucose utilization, and thus energy metabolism and physiological function, in the vestibular area of the brain. Sequential, double-label 2-DG injections in Bolivian squirrel monkeys revealed significant ratio ($p < 0.05$) increases in 2-DG uptake in six motion-stimulated animals as compared with six quiescent controls. Increased 2-DG uptake occurred in the medial and inferior vestibular nuclei (termination of afferents from the inner ear) and the nucleus cuneatus (termination of some afferents from the spinal cord). More recent densitometric studies of autoradiographs in six subjects showed (as expected) selectively greater uptake by all vestibular nuclei and the nucleus prepositus in rotated subjects than in quiescent subjects. The inferior olivary nucleus and lateral cuneate nuclei somewhat unexpectedly showed enhanced glucose utilization in response to motion stimuli.

In another study, utriculo-sacculotomy (which eliminates input from the otolith organs but spares that from the semicircular canals) in three motion-emetic sensitive animals rendered them resistant to motion-emetic stimuli. Area postremectomy by aspiration also rendered three subjects refractory to motion-emetic stimuli.

In a third study the vestibulo-ocular reflex and the susceptibility to motion sickness were compared in 16 subjects (Fig.14). Animals with the most sensitive vestibulo-ocular reflexes were least sensitive to motion sickness, and their vestibulo-ocular reflex habituated more slowly than in motion-emetic sensitive subjects.

In a fourth study ^3H -spiperone (^3H -S) binding sites to (D2) receptors in the brain stem were very numerous in bovine area postrema (AP) and vagal nuclear complex. The reticular formation and the vestibular nuclei, however, have a much lower number of binding sites. Binding of ^3H -S was inhibited in the AP by the anti-emetic drugs chlorpromazine, thiethylperazine, and domperidone.

Publications: Brizzee, K.R., and W.P. Dunlap. 1983. "Motion-induced alterations in 2-deoxyglucose uptake in brainstem nuclei of squirrel monkeys: Autoradiographic and liquid scintillation studies." BRAIN, BEHAVIOR AND EVOLUTION 23: 14-25.

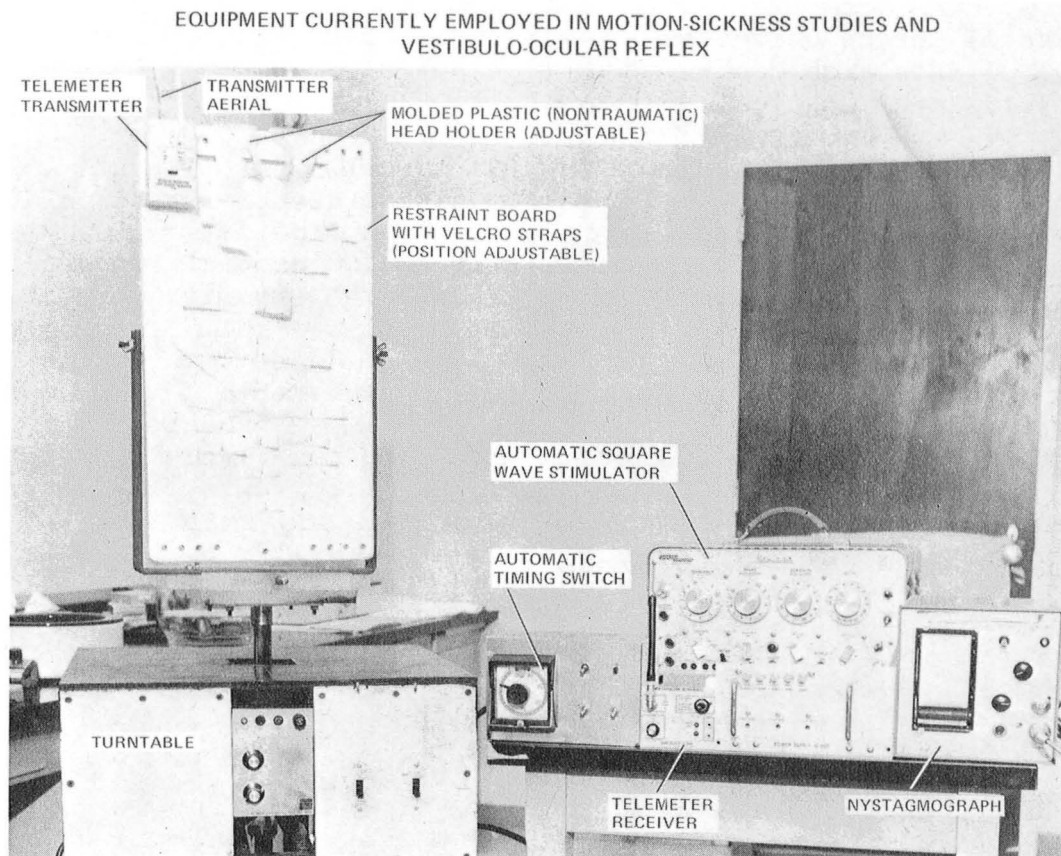


Fig. 14. (Brizzee 199-20-22-11)

V.J. Wilson, Rockefeller University, New York
N.G. Daunton, Ames Technical Monitor

Experimenters sought a better understanding of vestibular function in the cat. Neurons were studied in the lateral vestibular nucleus of cats, responding to three-dimensional stimuli. The neurons possessed a response vector tuned to a particular direction of vertical tilt. The response to any direction of tilt was proportional to the cosine of the angle between the applied stimulus and the response vector.

In other studies the dynamics of the tonic neck reflex showed a phasic component in forelimb extensors (muscles that contract and straighten the limb). This phasic component was revealed by a gain increase, and sometimes by a phase advance. Linear, vectorial addition was found between vestibular and neck reflexes over the frequency that this interaction could be studied, i.e., 0.05-0.5 Hz. In the cervical enlargement of the spinal cord, interneurons responded to neck and vestibular stimulation in a way similar to responses during forelimb reflex stimulation. Some interneurons may be in a combined neck-vestibular pathway to forelimb motor-neurons (Fig. 15).

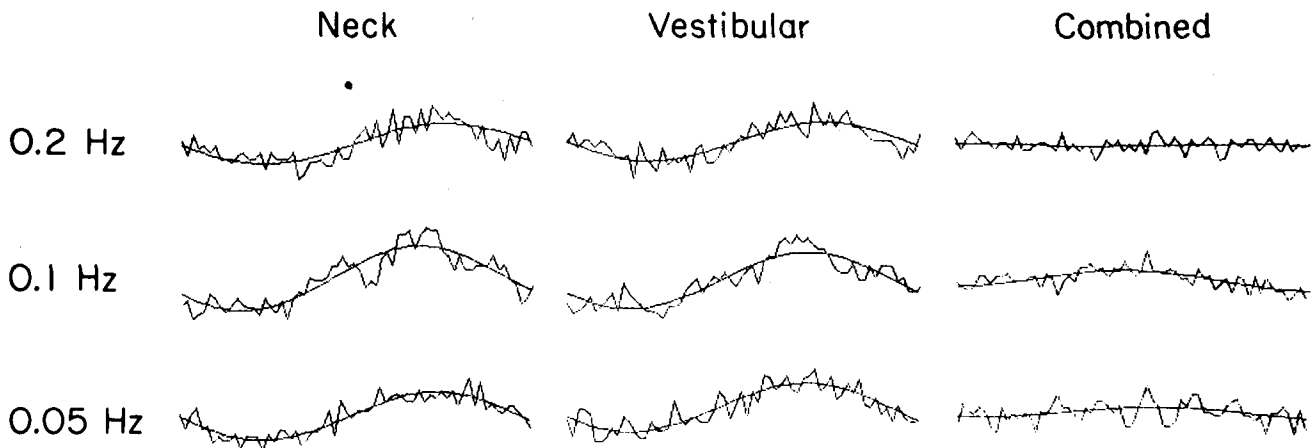


Fig. 15. Graphic representation of an averaged cycle from cervical interneurons in decerebrate cats, responding to sinusoidal stimulation of: (1) neck receptors when the body was rotated in the roll axis with the head fixed, (2) vestibular receptors when the whole body was rolled, and (3) neck and vestibular receptors combined when only the head was rotated. Responses of neck and vestibular stimulation were opposite in polarity. Excitation occurred by rotating the ipsilateral side toward the chin, or by rotating the body ipsilaterally ear down. When only the head was rotated, activating both the neck and vestibular receptors, little or no modulation resulted. This type of neuron is perhaps part of a combined neck and vestibular reflex pathway to motoneurons. (Wilson 199-20-22-14)

In motion sickness studies investigators obtained evidence indicating that the posterior cerebellar vermis (linking the two hemispheres of the cerebellum) is not an obligatory part of the pathway producing vestibular-induced vomiting.

Publications: (1) Baker, J., J. Goldberg, B. Peterson, and R. Schor. 1982. "Oculomotor reflexes after semicircular canal plugging in cats." *BRAIN RESEARCH* 252: 151-155. (2) Ezure, K. and V.J. Wilson. 1983. "Dynamics of neck-to-forelimb reflexes in the decerebrate cat." *JOURNAL OF NEUROPHYSIOLOGY* 50(3): 688-695. (3) Ezure, K., K. Fukushima, R.H. Schor, and V.J. Wilson. 1983. "Compartmentalization of the cervicocollic reflex in cat splenius muscle." *EXPERIMENTAL BRAIN RESEARCH* 51: 397-404. (4) Miller, A.D., P.S. Roossin, and R.H. Schor. 1982. "Roll tilt reflexes after vestibulospinal tract lesions." *EXPERIMENTAL BRAIN RESEARCH* 48: 107-112. (5) Miller, A.D. and V.J. Wilson. 1983. "Vomiting center reanalyzed: An electrical stimulation study." *BRAIN RESEARCH* 270: 154-158.

CENTRAL OTOLITH MECHANISMS IN THE SQUIRREL MONKEY 199-20-22-15

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N.G. Daunton, Ames Technical Monitor

Neurophysiological investigations were made of the spontaneous activity of vestibular canal afferents in gerbils. A significant percentage of canal afferents responded to changes in linear acceleration, especially afferents that exhibited an irregular spontaneous firing rate. In addition canal afferent activity in the anesthetized animal was significantly slower than in unanesthetized animals.

A second series of experiments were conducted to trace the neural projections of vestibular afferents that innervate each sensory organ of the labyrinth. To label cell bodies and processes, neuronal tracer substances were injected into different regions of the sensory neuroepithelium (the lining of cells in the vestibular organs of the inner ear) or into individual axons. A new procedure was developed to preserve the delicate afferent connections of the first order vestibular neurons (those neurons from the inner ear) along with the connection of Scarpa's ganglion to the brainstem. Connections were traced from the injection site to axonal terminations within the brain's vestibular nuclei.

Neural processes of compensation to loss of vestibular function on one side of the body were also investigated. The influence of somatosensory spinal cord input to the vestibular nuclei was evaluated in gerbils. Changes in spontaneous activity and dynamic responses were measured in neurons of the medial and vestibular nuclei during horizontal angular acceleration during compensation. Somatosensory input from the spinal cord to the vestibular nuclei was necessary to compensate for the removal of one vestibular labyrinth.

Publications: Perachio, A., and M. Correia. 1983. "Responses of semicircular canal and otolith afferents to small angle static head tilts in the gerbil." *BRAIN RESEARCH* 280: 287-298.

E. Bizzi, Massachusetts Institute of Technology, Cambridge, Department of Psychology
N.G. Daunton, Ames Technical Monitor

Discharge patterns were recorded from neurons in the brain stem's pons of alert monkeys (*Macaca mulatta*) trained to make head movements to visible targets. Special instrumentation was designed to monitor both horizontal and vertical head movements. Investigators devised a way to stimulate, separately, the neck proprioceptive system and the vestibular system, while recording single cell activity in the brain stem. Chronic implants were also developed in the spinal cord to identify the projection of head-related cells. Signals were recorded in the pontine reticular formation (PRF). A variety of cells were found related to movements of the arm, head, torso, mouth, tongue, and eyes. The medial area of the PRF, particularly those lying just below the VI nucleus, contained a small number of head-related cells. Some of these cells fired during horizontal head velocity in one direction and paused during head movements in the opposite direction. Other neurons discharged prior to and during head movements in one direction, but they also showed some activity during movements in the opposite direction. Also found were a few cells whose discharge is related to head position. These cells do not seem to be affected by concomitant eye saccades (quick movements). Some of these head-related cells received vestibular afferent information, and a few received input from neck receptors.

Although the technically demanding task of recording single neurons from the brain stem of alert monkeys was mastered, only a small number of head-related cells were encountered. In general, the few cells that related to head movement were not grouped, but rather seemed to be dispersed in the reticular formation. (This task was successfully completed and terminated.)

Publications: (1) Bizzi, E. 1983. "Central processes involved in arm movement control." in *The Production of Speech*. MacNeilage, P.F., ed. New York: Springer-Verlag. pp. 3-10. (2) Bizzi, E., and W. Bend. 1983. "Posture control and trajectory formation in single and multiple joint arm movements." in *Motor Control Mechanisms in Health and Disease*. Desmedt, J.E., ed. New York: Raven. pp. 31-45. (3) Bizzi, E., W. Chapple, and N. Hogan. 1982. "Mechanical properties of muscles: Implications for motor control." *TRENDS IN NEUROSCIENCE* 5(11): 395-398. (4) Lestienne, F., and E. Bizzi. 1982. "Processus de controle du mouvement et de sa position finale au cours d'une tache de pointage." in *Elements de Neurobiologie des Comportements Moteurs*. Azemar, G., and H. Ripoll, eds. Paris: I.N.S.E.P. pp. 101-122. (5) Lestienne, F., D. Whittington, and E. Bizzi. 1983. "The coordination of eye-head movements in alert monkeys: Behavior of eye-related neurons in the brain stem." in *Spatially Oriented Behavior*. Hein, A. and M. Jeannerod, eds. New York: Springer-Verlag. pp. 105-118.

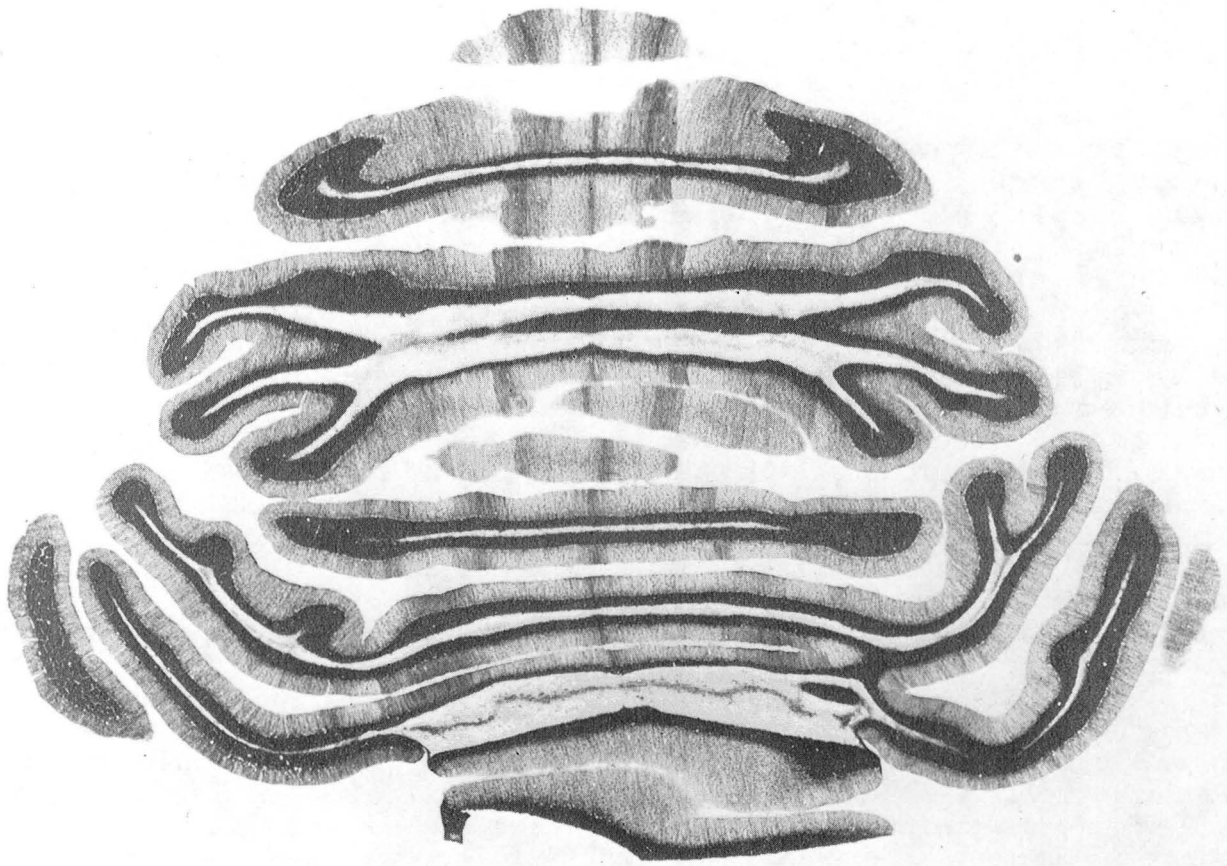


Fig. 16. Acetylcholinesterase band-pattern in the cerebellum of the cat. (Graybiel 199-20-22-18)

VESTIBULO-CEREBELLAR ANATOMY AND HISTOCHEMISTRY: A STUDY OF NEURAL STRUCTURES UNDERLYING MOTION SICKNESS 199-20-22-18

A.M. Graybiel, Massachusetts Institute of Technology, Cambridge, Department of Psychology and Brain Science

W.R. Mehler, Ames Technical Monitor

The enzyme, acetylcholinesterase (AChE), is basic to the functioning of the central nervous system. AChE activity follows the nerve's cholinergic reaction, liberating acetylcholine to assist in electrical transmission at nerve synapses and neuro-muscular junctions. AChE decomposes acetylcholine to prevent uncontrolled re-excitement of the nerve.

Staining revealed striking longitudinal bands of high and low AChE activity visible in the molecular layer of adult cat cerebellum (Fig. 16). The edges of certain bands marked the boundaries of Voogd's A and B connectional zones. In particular, the most medial AChE-rich band marked the location of the Purkinje cells projecting to the fastigial nucleus. The next lateral band marked the location of the vermal Purkinje cells, projecting into the complex of vestibular nuclei.

In the early postnatal period, the cerebello-vestibular structure should be open to external influences during the final modeling of the connections. (The longitudinal organization of the cerebellum appears to develop early, as elongated clusters of neurons were observed prenatally by Korneliussen in 1969.)

We also continued to study thalamic and basal ganglia circuitry, which link various motor pathways, in relation to their possible roles in postural mechanisms, visuo-oculomotor control, and the pharmacology of motion sickness. One of the most striking findings was a tight correlation between the distribution of dopamine-containing fibers and acetylcholine-binding sites in the striatum. This finding may bear on cholinergic-dopaminergic interactions in the striatum. Because a cholinergic-adrenergic imbalance had been proposed as the prelude to motion sickness and since dopaminergic mechanisms may be induced in triggering motion sickness, these findings should increase our understanding of processes controlling orientation, movement and physiological homeostasis in spaceflight.

Publications: (1) Berson, D.M., and A.M. Graybiel. 1983. "Organization of the striate-recipient zone of the cat's lateralis posterior-pulvinar complex and its relations with the geniculostriate system." *NEUROSCIENCE* 9(2): 337-372. (2) Edley, S.M., and A.M. Graybiel. 1983. "The afferent and efferent connections of the feline nucleus tegmenti pedunculopontinus pars compacta." *JOURNAL OF COMPARATIVE NEUROLOGY* 217: 187-215. (3) Graybiel, A.M., and R.P. Elde. 1983. "Somatostatin-like immunoreactivity characterizes neurons of the nucleus reticularis thalami in the cat and monkey." *JOURNAL OF NEUROSCIENCE* 3(6): 1308-1321. (4) Graybiel, A.M., and C.W. Ragsdale, Jr. 1983. "Biochemical Anatomy of the Striatum." in *Chemical Neuroanatomy*. Emson, P.C., ed. New York: Raven. pp 427-504. (5) Oertel, W.H., A.M. Graybiel, E. Mugnaini, R.P. Elde, D.E. Schmechel, and I.J. Kopin. 1983. "Coexistence of glutamic acid decarboxylase- and somatostatin-like immunoreactivity in neurons of the feline nucleus reticularis thalami." *JOURNAL OF NEUROSCIENCE* 3(6): 1322-1332.

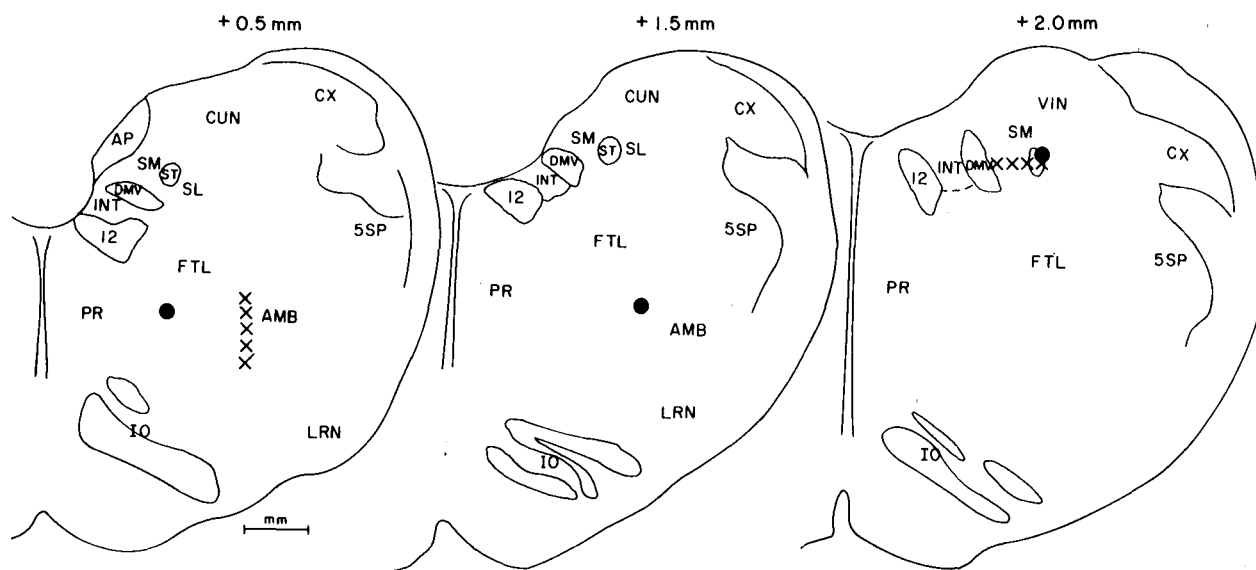


Fig. 17. Electrical stimulation of the brain stem in the cat was used to find a restricted localization of a "vomiting center." Vomiting was produced only once during stimulation in each of three animals; the sites are shown in the illustration by black dots in the lower brain stem. Vomiting-like behavior, or retching, without expulsion of gastric contents, was obtained in two other animals at sites marked with an X. Numerous attempts to produce vomiting by stimulation in these regions proved unsuccessful in animals that were either susceptible or non-susceptible to motion-induced vomiting. Restricted localization of a "vomiting center" that evokes a reproducible response when stimulated could not be obtained. Abbreviations: AMB - nucleus (n.) ambiguus, AP - area postrema, CUN - cuneate n., CX - external cuneate n., DMV - dorsal motor n. of vagus, FTL - lateral tegmental field, INT - n. Inter-calatus, IO - inferior olive, LRN - lateral reticular n., PR - paramedian reticular n., SL - lateral solitary n., SM - medial solitary n., ST - solitary tract, VIN - descending vestibular n., 5SP - spinal trigeminal n., I2 - hypoglossal n. (Miller 199-20-22-21)

PHYSIOLOGY OF CAT VESTIBULAR SYSTEM EFFERENT NEURONS 199-20-22-20

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Department of Physiology
N.G. Daunton, Ames Technical Monitor

The investigator continued to develop and refine training procedures for producing yaw (left-right rotational) sinusoidal head movements from awake cats, who could freely move their heads. Using water as a reward, each cat tracked a servo-driven, sinusoidally-oscillating drinking tube. A rotary potentiometer attached to the head monitored movement. Hardware was also implemented to record eye movements of cats using silver/silver chloride electrodes, and computer software was developed to analyze the data. Horizontal eye movements were characterized during voluntary sinusoidal head movements at a variety of frequencies and amplitudes in the horizontal plane. In addition, spontaneous head and eye movements (yaw) were characterized, as well as those movements evoked passively (controlled by the experimenter). Progress was made in developing procedures for recording the activity of physiologically-defined vestibular efferent neurons and primary afferents in these animals during voluntary sinusoidal, passively-imposed, and spontaneous head movements.

Publications: none

VESTIBULAR SYSTEM AND NEURAL CORRELATES OF MOTION SICKNESS 199-20-22-21

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N.G. Daunton, Ames Technical Monitor

Because a restricted, localized vomiting center could not be found using electrical stimulation in the brain stem of the cat (Fig.17), experiments were begun to investigate the brain stem control of the abdominal muscles and diaphragm that are primarily responsible for producing the pressure changes required for vomiting. The motoneurons that innervate the abdominal muscles were stained and localized using the retrograde transport of horseradish peroxidase. A great variation was found in the rostral extent of the motoneuron pools supplying the different muscles. The types and locations of neurons in the dorsal and ventral respiratory groups that project to the lumbar portion of the spinal cord were investigated in 14 cats. This region of the cord was chosen for study because the abdominal muscles receive part of their innervation from this level, while the other major respiratory muscles are innervated from higher (rostral) segments.

Publications: Miller, A.D., and V.J. Wilson. 1983. "Vomiting center reanalyzed: An electrical stimulation study." BRAIN RESEARCH 270: 154-158.

INVESTIGATIONS OF VESTIBULAR RESPONSE DYNAMICS USING THE VESTIBULAR RESEARCH FACILITY (VRF) 199-20-22-22

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Otolaryngology
N.G. Daunton, Ames Technical Monitor

As part of the task to evaluate the effects of dynamic linear acceleration on vestibular function using the Vestibular Research Facility (VRF) at Ames Research Center (ARC), a chronically instrumented, behaving gerbil preparation was developed. Integration of the gerbil preparation into the VRF and development of a body restraint system progressed smoothly. Preliminary data gathered using the linear translator at the University of Texas Medical Branch preceded experiments at ARC. Experiments on the VRF centrifuge at ARC were initiated.

Publications: none

ROLE OF BIOCHEMICAL FACTORS IN MOTION SICKNESS 199-20-22-23

G.H. Crampton, Wright State University, Dayton, OH, Department of
Psychology
N.G. Daunton, Ames Technical Monitor

Collection of data evaluating the drugs droperidol and domeridone was completed. Droperidol, a dopamine antagonist that crosses the blood-brain barrier, was effective in preventing motion sickness in the cat. Domperidone, a dopamine antagonist that does not cross the blood-brain barrier, failed to be effective against sickness.

Analyses began of cerebrospinal fluid (CSF) in the cat before, during and after motion stress, although only non-susceptible (to motion sickness) cats were tested. We were able to place long-dwelling, chronic cannulae in the third and fourth ventricles (CSF-containing core of the brain), as well as in the cisterna magna (space between the cerebellum and medulla oblongata). Other developments included the design, construction and testing of a new device to produce motion sickness that is quiet and economical (two animals can be tested at the same time). A means of sampling CSF from the unrestrained cat during motion testing was designed and fabricated.

Publications: (1) Crampton, G.H., and N.G. Daunton. 1983. "Evidence for a motion sickness agent in cerebrospinal fluid." BRAIN, BEHAVIOR AND EVOLUTION 23: 36-41. (2) Crampton, G.H., and N.G. Daunton. 1983. "Systemic naloxone increases the incidence of motion sickness in the cat." PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR 19: 827-829.

BONE ALTERATIONS

Despite an adequate diet and daily physical exercise, astronauts lost body calcium and bone mass during the Skylab flights of two to three months duration in the early 1970s. Russian cosmonauts lost 3.2% to 7.0% of bone mineral content during flights of six months duration. Typically, weightlessness primarily affected the weight-bearing bones. The pattern of recovery after flight remained poorly defined and weakening of the skeleton continued to be a possible hazard. The consequences of space osteoporosis for passengers and crew members in future, long duration missions and from successive exposures to spaceflight were not determined.

Animals showed similar changes during flight in Soviet Cosmos biosatellites. Dogs lost mineral content in their legs. Three weeks of weightlessness in the young, growing rat arrested growth of the osteoblasts (bone-forming cells) in the leg bones, while bone resorption by osteoclasts continued normally. (Osteoblasts form a contiguous layer, covering the bone matrix; osteoclasts have long projections across the surface of the bone to resorb any exposed matrix.) In addition rhesus monkeys immobilized in a semi-reclined position showed a loss of compact bone.

The metabolic data derived from Skylab experiments suggest the possibility that intestinal malabsorption of calcium may be one mechanism contributing to bone mineral loss. The homeostatic mechanisms of the response would include alterations in serum level of two potent bone resorbing factors (1,25-dihydroxyvitamin D₃ and parathyroid hormone), which induce bone loss. State-of-the-art ground-based models of adult-acquired osteoporosis suggest that reversible osteoporosis is associated with increased activation of remodeling, resorption, and bone turnover. Thus, adult-acquired osteoporosis may be prevented by suppressing the number of active remodeling sites.

The need is clear for a responsive experimental model of reversible adult-acquired osteoporosis to elaborate and define alterations of intestinal absorption, and the relationship with bone-remodeling regulatory factors and calcium homeostasis. Interdisciplinary investigations have been undertaken to develop a nonhuman primate model with bone remodeling functions similar to those observed in humans.

D.R. Young, Ames Research Center, Biomedical Research Division

Chronic immobilization of adult, male pigtail monkeys (Macaca nemestrina) resulted in a loss of cortical bone in the normally weight-bearing portions of the appendages, and a chronic metabolic alkalosis reflected in higher than normal urinary acid excretion and increased blood pH and bicarbonate levels. Following re-ambulation, the recovery of bone was slow requiring many months, although the alkalosis reversed rapidly. Early signs of bone loss in the tibia occurred within one month of immobilization. Large portions of osteons underwent structural and compositional changes, which is thought to be the initial stages of resorption cavity formation. The remaining tissue then demineralized. Because a decrease in bone bending stiffness also occurred, the response to a hypodynamic, weightless environment could have serious consequences. Three patterns of recovery included massive new bone growth with re-filling of resorption cavities, re-mineralization of older bone, and apposition of lamellar bone on the periosteum, the connective tissue with bone-forming potential that covers all healthy bones.

The responses of experimental primates to nine days of immobilization were similar to responses in astronauts, as well as responses of humans with diseases associated with secondary hyperaldosteronism, characterized by alkalosis and an excessive secretion of aldosterone. Administration of mineralocorticoids to normal animals altered the pattern of acid-base regulation, but did not simulate the changes seen in immobilized primates. Consequently, the alterations in experimental animals probably reflected the influence of multiple factors of immobilization.

Further research was undertaken to: elucidate effects of parathyroid hormone (parathormone) on acidification in bone relating to the resorptive process, evaluate fluctuations of tissue levels of osteocalcin as a marker for bone remodeling events, study the influence of local and hormonal remodeling regulatory factors, and examine changes in bone collagen and crystalline phase during bone loss and subsequent recovery. Reports showed that parathyroid activity influenced bone turnover, skeletal mobilization, and acid-base homeostasis. Manipulation of dietary calcium or vitamin D was considered as a potential means of changing the blood level of parathyroid hormone. In collaboration with S. Arnaud of the San Francisco Veterans' Administration Hospital, studies with experimental monkeys were undertaken to establish the feasibility of altering serum levels of parathormone. The response of adolescent and old animals to a low calcium diet was similar (Table III). Experiments were initiated to determine serum parathormone levels during immobilization.

Publications: (1) Young, D.R., W.J. Niklowitz, and C.R. Steele. 1983. "Tibial changes in experimental disuse osteoporosis in the monkey." CALCIFIED TISSUE INTERNATIONAL 35(3): 304-308. (2) Young, D.R., I. Yeh, and R.S. Swenson. 1983. "Metabolic alkalosis during immobilization in monkeys (M. nemestrina)." CALCIFIED TISSUE INTERNATIONAL 35(4-5): 472-476.

TABLE III. EFFECT OF A LOW CALCIUM DIET ON SERUM IMMUNOREACTIVE
PARATHORMONE
(Young 199-20-32-01)

<u>Diet</u>	<u>Serum PTH, pg/ml</u>
high calcium	126
low calcium	240

BONE ELASTICITY 199-20-32-02

C.R. Steele, Stanford University, Department of Mechanical Engineering
D.R. Young, Ames Technical Monitor

A test using a noninvasive impedance probe was designed to determine bone stiffness across the length of the long bones (ulna, radius, and tibia), which are affected by osteoporosis during spaceflight and on Earth. Calibrations were conducted on proof masses, and the algorithm for determination of bone stiffness and mass was confirmed on a series of standards with simulation of skin and soft tissue. Measures of the gross bending stiffness of the tibia and ulna were demonstrated in humans. Tests to establish normative population values were also conducted. Measurements were also made on the immobilized monkey (Macaca nemestrina), and evaluated in relationship to microscopic and mineral changes in the cortical portion of the bone. Following six months of restraint in seven monkeys, the greatest loss of bone mineral in the tibia ranged from 23% to 31%; the largest changes in bone stiffness ranged from 36% to 40%. Approximately 8.5 months of recovery was required for restoration of normal bending properties, although bone mineral content did not necessarily return to normal levels.

Publications: Young, D.R., W.J. Niklowitz, and C.R. Steele. 1983. "Tibial changes in experimental disuse osteoporosis in the monkey." CALCIFIED TISSUE INTERNATIONAL 35(3): 304-308.

CALCIUM HOMEOSTASIS IN ALTERED GRAVITY 199-20-32-06

E.M. Holton, Ames Research Center, Biomedical Research Division

Evidence from prolonged spaceflight suggested that excessive steroid secretion from the adrenal cortex or increased sensitivity to steroids by target cells, such as osteoblasts (OB), may contribute to reduced bone formation. Rats and mice exhibited different responses to dexamethasone, a synthetic glucocorticoid. Dexamethasone inhibited receptors for the active metabolite of vitamin D ($1,25(\text{OH})_2\text{D}_3$) and slowed cell division at all growth phases of mouse OB. On the other hand, dexamethasone increased the number of vitamin D receptors in the rat. The effect on rat OB was dependent on the cells' period of growth. Dexamethasone inhibited growth

in rat cultures when cells were sparse, had no effect on intermediate densities, and stimulated growth in mixed cultures. (This task was successfully completed and terminated.)

Publications: Chen, T.L., C.M. Cone, E.M. Holton, and D. Feldman. 1983. "1,25-dihydroxyvitamin D₃ receptors in cultured rat osteoblast-like cells: Glucocorticoid treatment increases receptor content." JOURNAL OF BIOLOGICAL CHEMISTRY 258(7): 4350-4355.

PHARMACOLOGICAL PREVENTION OF BONE LOSS 199-20-32-14

A.D. Kenny, Department of Pharmacology and Therapeutics, Texas Tech University Health Sciences Center, Lubbock, TX.

D.R. Young, Ames Technical Monitor

Parathyroid hormone (PTH) caused a release of calcium from bone tissue by acting on the osteoblasts, or bone-forming cells. In addition to hypercalcemia (excess calcium in the blood), synthetic bovine PTH relaxed the blood vessels, causing hypotension. Mild oxidation of bovine PTH with hydrogen peroxide eliminated the hypotensive effect. Apparently, the portion of the peptide of the PTH molecule for vascular action was no longer accessible to the receptors of target organs, while the peptide portion causing hypercalcemia was unaffected.

PTH also increased 2 to 3 times the level of carbonic anhydrase, the enzyme that aids the transfer of CO₂ from tissue to blood to the air. Acetazolamide, a renal carbonic anhydrase inhibitor, blocked PTH mobilization of calcium out of the bone, thus preventing disuse osteoporosis in the rat. PTH also increased by 50% acid phosphatase, which is active in the liberation from phosphoric acid of phosphate ions used by the body in converting ADP to ATP for energy storage.

Publications: Pang, P.K.T., M.C.M. Yang, H.T. Keutmann, and A.D. Kenny. 1983. "Structure activity relationship of parathyroid hormone separation of the hypotensive and hypercalcemic properties." ENDOCRINOLOGY 112: 284-289.

OSTEOCALCIN IN BONE, AND ITS ROLE IN CALCIUM HOMEOSTASIS 199-20-32-15

P.X. Callahan, Ames Research Center, Biosystems Division

P. Patterson-Allen, University of California, San Francisco, Department of Radiology

Osteocalcin (OC) is the second most abundant protein in bone and makes up 1% to 2% of the total protein. The specific function of OC has yet to be defined, but it does accumulate in the extracellular matrix of bone. OC binds to hydroxyapatite during the early stages of new mineralization (see p. 74, 199-20-32-19). OC appears concomitant with the calcification of bone, and increases proportionately as hydroxyapatite is deposited. OC in bone is dependent on vitamin K, and is released into blood and urine during bone turnover. Blood levels of OC are increased by vitamin D and parathyroid hormone, and decreased by glucocorticoid therapy, calcitonin and

reduced parathyroid function. Purified OC appears to break down under normal storage conditions in the laboratory and should be handled with care.

Immunoassays were developed to detect the calcium-binding protein, osteocalcin. Urine levels increased dramatically with the onset of restraint in the monkey (*Macaca nemestrina*) (Fig. 18). OC levels were not related to increased urinary aldosterone in the same animals, as demonstrated in studies using injections of desoxy-corticosterone acetate. Serum OC levels decreased in both young and old rats under cold stress (from 2 hours to 3 weeks), restraint, centrifugation, and change of cage environment. Suspension of the hind limbs of rats produced an initial decrease in serum OC, which appeared to reflect the stress of the suspension procedure. After adaptation of the rats to suspension, the serum OC stabilized near control levels, while formation rate consistently decreased in the unloaded limbs. Daily samplings of rat (male and female) and human serum, as well as human and monkey urine, showed considerable fluctuation of OC levels, suggesting caution in the use of a single measure as an indicator of bone metabolism, especially in a stressed subject. In summary, laboratory research showed that various forms of stress (change of temperature, environment, or musculo-skeletal loading) altered the circulating levels of osteocalcin, which can be measured further in astronauts or flight animals with the assay developed. (This task was successfully completed and terminated.)

Publications: Lian, J.B., G. Boivin, P. Patterson-Allen, M. Grynpas, and C. Walzer. 1983. "Calcery and calciphyllaxis: Timed appearance of gamma-carboxyglutamic acid and osteocalcin in mineral deposits." *CALCIFIED TISSUE INTERNATIONAL* 35: 555-561.

MECHANISMS OF ACTION OF GLUCOCORTICOSTEROIDS AND FLUORIDE ION ON THE GROWING SKELETON 199-20-32-18

W.S. Jee, University of Utah School of Medicine, Department of Pharmacology
D.R. Young, Ames Technical Monitor

Age-related osteoporosis is believed to be associated with changes in normal bone remodeling and tissue turnover. Reversible osteoporosis from spaceflight, bedrest or immobilization, is associated with an increased number and frequency of remodeling events and a progressive loss of bone. Several hormones are remodeling agents; some depress activation of bone remodeling (Haversian) units, and others increase Haversian activation. Studies seek the causes and prevention of reversible osteoporosis.

Regulatory factors were studied to evaluate their effect on bone structure and mineral metabolism and to gain insight into their mechanisms of action. Warfarin, a vitamin K antagonist administered daily to weanling rats during their first two months after birth, caused a decrease in gamma-carboxyglutamate, the major calcium-binding protein in bone. Fusion with the joint at the end of the tibia and cessation of growth resulted. In another study the glucocorticoid, cortisol, suppressed the remodeling rate of bone, causing a decline in the bone resorption, formation and apposition rates (Fig. 19) in both the vertebrae and the tibia. On the other hand,

**24-HOUR URINARY OSTEOCALCIN LEVELS IN RESTRAINED
AND CONTROLLED MACACA NEMESTRINA**

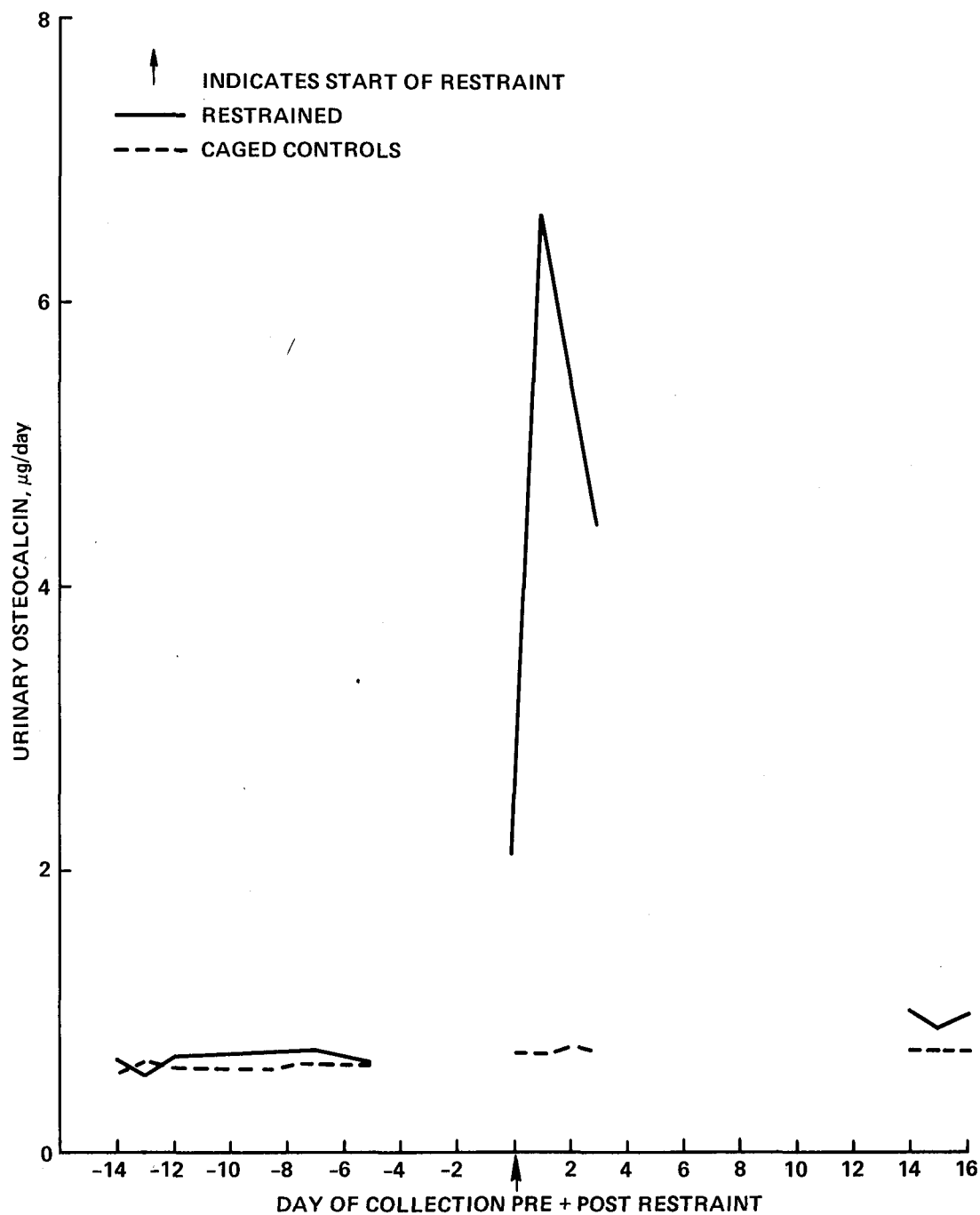


Fig. 18. (Callahan and Patterson Allen 199-20-32-15)

APPOSITION AND RESORPTION OF CORTICAL BONE FROM THE CAUDAL VERTEBRAE OF FEMALE WEANLING RATS TREATED WITH CORTISOL FOR 7 DAYS

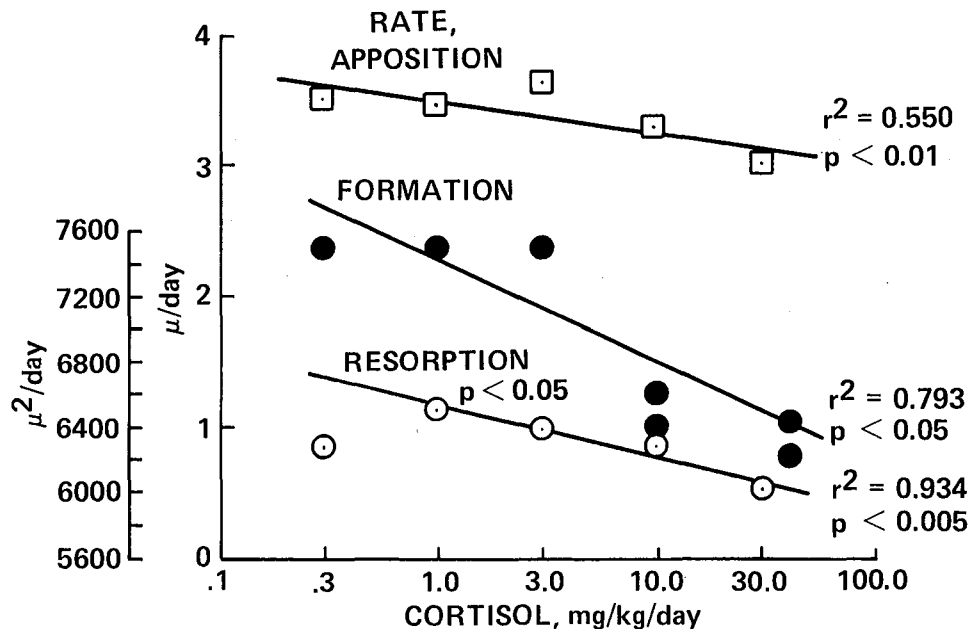


Fig. 19. Dose-effect curves of endosteal bone resorption rate, and periosteal bone apposition and formation rates in cross sections of caudal vertebrae. The bone resorption rate was significantly elevated compared to control animals at doses of 1.0 mg/kg/day. Resorption rate was significantly less than controls at 30 mg/kg/day, along with bone apposition.

Ordinate scales: μ^2/day used for apposition and resorption rates; μ/day used for the formation rate. (Jee 199-20-32-18)

prostaglandins stimulated the remodeling events and increased the percentage of hard tissue in the proximal tibia. Stimulation of new bone formation should be useful in the bone healing process, particularly in the restitution of trabecular bone in skeletally-depleted individuals.

Publications: (1) Jee, W.S.S., T. Wronski, E.R. Morey, and D.B. Kimmel. 1983. "The effects of space flight on trabecular bone in rats." AMERICAN JOURNAL OF PHYSIOLOGY 244: R310-R314. (2) Price, P.A., M.K. Williamson, T. Haba, R.B. Dell, and W.S.S. Jee. 1982. "Excessive mineralization with growth plate closure in rats on chronic warfarin treatment." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA 79(24): 7734-7738.

ELECTRON PROBE ANALYSIS OF TRABECULAR AND CORTICAL BONE 199-20-32-19

T.E. Bunch, Ames Research Center, Extraterrestrial Research Division
D.R. Young, Ames Technical Monitor

Following immobilization of a nonhuman primate (Macaca nemestrina) and a period of normal recovery, cortical bone was evaluated by microradiography, and the results correlated with electron probe analysis. Young osteons contained approximately 18% less mineral than older osteons. During bone resorption there was a non-specific mineral loss of 2% to 5% from all osteons. Less mineral was seen at the Haversian canals than in the area radiating outward through the osteon to the cement line. During recovery from osteoporosis, newly-formed osteons had a higher than normal ratio of calcium to phosphorus and lesser amounts of fluorine. The studies provided evidence that new bone formed during recovery contains mostly precursors of hydroxyapatite crystals.

Publications: none

BIOCHEMICAL CHANGES IN BONE IN A MODEL OF WEIGHTLESSNESS 199-20-32-20

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D.R. Young, Ames Technical Monitor

In eight samples supplied by Ames Research Center the bone from immobilized monkeys (Macaca nemestrina) contained more non-mineralized collagen matrix than controls or animals recovering from immobilization. (Control animals had about 20% non-mineralized collagen in their bone.) After 11 months of recovery in a 10-week immobilized monkey only limited mineralized collagen was observed. The mineralized collagen appeared in recovered animals because of new collagen synthesis with its subsequent mineralization. Not all of the old non-mineralized collagen disappeared, possibly due to its greater resistance to degradation caused by increase pyridinum (C_5H_6N) crosslinks.

Work began on using a tendonectomized rat to study disuse osteoporosis. Our preliminary study used photon absorptiometry to measure bone mineral content in tibias and femurs from four rats, which were subjected to knee tendonectomies. The animals were Holtzman male rats, which had their left knee joint tendonectomized at a weight of 180 g. The animals did not use their left hind leg during the entire two-week period following tendonectomy, and weighed 290 g at the end of the period. This weight gain was normal for the animals. The bones were excised from the rats and cleaned. The right tibias and femurs served as contralateral controls for the measurements. The bone was measured across the shaft at increments of the diameter of the collimated photon beam (3.175 mm). Bone mineral content was 8.5% lower in tendonectomized tibias and 16.7% lower in femurs, than in the control contralateral bones. Four sham operated rats did not show any right-left differences. The results are consistent with the dry weights of the bones obtained by Dr. Gideon Rodan of the University of Connecticut using the tendonectomized rat.

**IDENTIFICATION OF AN UNKNOWN HUMORAL AGENT RESPONSIBLE FOR BONE
MOBILIZATION 199-20-32-21**

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of Biochemistry

D.R. Young, Ames Technical Monitor

Experiments continued to determine the hormones responsible for mobilization of calcium from bone during lactation. Bromocryptine stopped both lactation and bone loss. Controlling administration of the hormone prolactin, secreted from the anterior pituitary, for experimental purposes could not be accomplished in pregnant rats due to many deaths and lactation failure following hypophysectomy (removal of the pituitary gland). However, it was discovered that prolactin secretion was highest in the mother at birth, while mineral loss from bone is highest midway during lactation. Therefore, it was unlikely that prolactin mobilized calcium from bone during lactation. Removal of the parathyroid gland from lactating rats did not reduce their bone loss even when they were fed a high calcium diet. (On a normal diet the animals died of tetany and could not be used to study the question.) Apparently, the parathyroids were not involved in the mobilization of calcium from bone resulting from lactation. Also, removal of the adrenals did not affect bone loss. By the elimination of prolactin, the adrenals, the parathyroids and vitamin D, an apparently unknown hormone caused the bone loss of lactation.

On a low calcium diet, rats were injected intraperitoneally daily with blood plasma taken from cows during their peak period of lactation. The blood calcium levels of the rats rose 1.5 to 2.0 mg/100 ml. Calcium levels remained at a normal level of 5.5 mg when rats were injected with plasma from non-lactating cows. The results suggested the existence of an unknown factor in lactating cows that mobilizes calcium.

Samples of plasma were analyzed from monkeys (*Macaca nemestrina*) immobilized at Ames Research Center. Surprisingly, 1,25-dihydroxy-vitamin D₃ levels were unexpectedly high (150 pg/ml). Plasma from non-immobilized control monkeys will be checked for comparison. Levels of the active forms of vitamin D, which normally mobilizes calcium from old bone, will also be measured in plasma taken from astronauts on the upcoming Shuttle-Spacelab 2 mission (see pg. 148).

Publications: (1) Chesney, R.W., R.B. Mazess, P. Rose, A.J. Hamstra, H.F. DeLuca, and A.L. Breed. 1983. "Long-term influence of calcitriol (1,25-dihydroxyvitamin D) and supplemental phosphate in x-linked hypophosphatemic rickets." PEDIATRICS 71: 559-567. (2) Honma, Y., M. Hozumi, E. Abe, K. Konno, M. Fukushima, S. Hata, Y. Nishii, H.F. DeLuca, and T. Suda. 1983. "1-alpha, 25-dihydroxyvitamin D₃ and 1 alpha-hydroxyvitamin D₃ prolong survival time of mice inoculated with myeloid leukemia cells." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA 80: 201-204. (3) Lindgren, J.U. and H.F. DeLuca. 1983. "Oral 1,25 (OH)₂D₃: An effective prophylactic treatment for glucocorticoid osteopenia in rats." CALCIFIED TISSUE INTERNATIONAL 35: 107-110. (4) Steinherz, R., R.W. Chesney, J.D. Schulman, H.F. DeLuca, and M. Phelps.

1983. "Circulating vitamin D metabolites in nephropathic cystinosis." JOURNAL OF PEDIATRICS 102: 592-594. (5) Stern, P.H., B.P. Halloran, H.F. DeLuca, and T.J. Hefley. 1983. "Responsiveness of vitamin D-deficient fetal rat limb bones to parathyroid hormone in culture." AMERICAN JOURNAL OF PHYSIOLOGY 244: E421-E424.

MUSCLE ATROPHY

Significant atrophy of skeletal muscle develops in both men and rats during spaceflight. In the late 1970s rats showed a 30% loss of mass in the soleus muscle of the hind limb following flight on joint US-USSR unmanned satellites. These flight data confirmed findings from the early 1970s of a 25% reduction in leg volume and strength of astronauts during 28 and 56-day missions of Skylab. Exercise on the last, 84-day Skylab flight cut the loss to 8%. Although exercise on a treadmill reduced the severity of the problem, muscle atrophy was not prevented entirely. Therefore, muscle atrophy remained a risk, particularly during longer missions required by astronauts for the construction and operation of a space station or a voyage to another planet.

Understanding the basic biochemical and physiological processes that regulate muscle mass and strength should precede the development of effective exercise, pharmacologic, and nutritional regimens to prevent atrophy. The fundamental processes regulating muscle mass and strength need to be investigated with biochemical techniques. Monitoring the loss of muscle mass and decrease in size will be done with cross-sectional x-rays from computerized axial tomography (CAT) scanning. In addition the technology of nuclear magnetic resonance (NMR), newly applied in biomedical research, appears extremely promising for monitoring the chemical, as well as the structural changes of soft tissue. NMR also avoids interference from injection of contrasting solutions, or exposing specimens to x-rays (see pg. 113).

Besides elucidating the mechanism of muscle atrophy, countermeasures may be achieved through identifying the action of specific types of exercise, applying electrical stimulation, and loading or stretching of muscles that are sensitive to gravity. These muscles include two basic types of fibers: the slow twitch and the fast twitch. Slow twitch fibers, which predominate in a muscle like the soleus, adapted through evolution for long, slow contraction to maintain posture. On the other hand, a muscle predominating in fast twitch fibers, like the gastrocnemius, developed with fewer fibers to contract for a shorter duration, thereby providing quick, accurate movements. In weightlessness, slow twitch fibers tend to convert to fast twitch, which fatigue sooner.

Investigators consider various hypotheses to explain the opposing functions which operate in concert to regulate muscle mass: the rate of protein biosynthesis, or anabolism, and the rate of protein degradation, or catabolism. Muscle mass increases in the presence of peptides, such as insulin growth factors (IGF), pancreatic insulin, and possibly other endogenous growth factors as yet unidentified. Steroids also affect protein turnover, although the process is poorly understood. In addition, immobilized muscle shows a decrease in number of glucocorticoid receptors. Recent studies have shown that protein synthesis and degradation is regulated by prostaglandins, and these processes can be dramatically modified by inhibitors of prostaglandin synthesis. Another hypothesis

concerns atrophy caused by severing the nerve from the muscle, which may prevent a biochemical, neurotrophic factor from regulating the rate of growth and breakdown via the neuromuscular junction.

Although disuse of muscle may cause a decrease in growth factors or receptors in muscle, biochemical inhibitors were also detected in fractions of serum and muscle fibroblasts. Proteases contained in cellular lysosomes appeared to act as a link in the atrophy process. Tripeptidyl aminopeptidase was successfully isolated from lysosomes and many of its properties were determined. Another protease, which is activated by the calcium (Ca^{2+}) content of the muscle, is located at the anchor points (Z-lines) of actin fibers in the muscle, an initial site of muscle degeneration. Another indication of the importance of proteolysis comes from the inhibition of muscle breakdown, both in vitro and in vivo, from a nontoxic microbial peptide, leupeptin.

Investigators can test these various hypotheses by employing tissue cultures of myoblasts. Other experiments are performed in vivo with rats physically immobilized in casts, or suspended by the hind limbs to remove the load on their muscles. Still other techniques include denervating specific muscles, severing the tendon between the muscle and the bone (tenotomy), and manipulating hormones through injections of glucocorticoids or inhibitors of prostaglandin synthesis. Because these methods can only simulate the effects of weightlessness on Earth, definitive tests will occur with experiments in space, such as the one scheduled on the upcoming flight of Shuttle-Spacelab 4.

CAF AND INHIBITOR ACTIVITY IN RAT TISSUE EXTRACTS

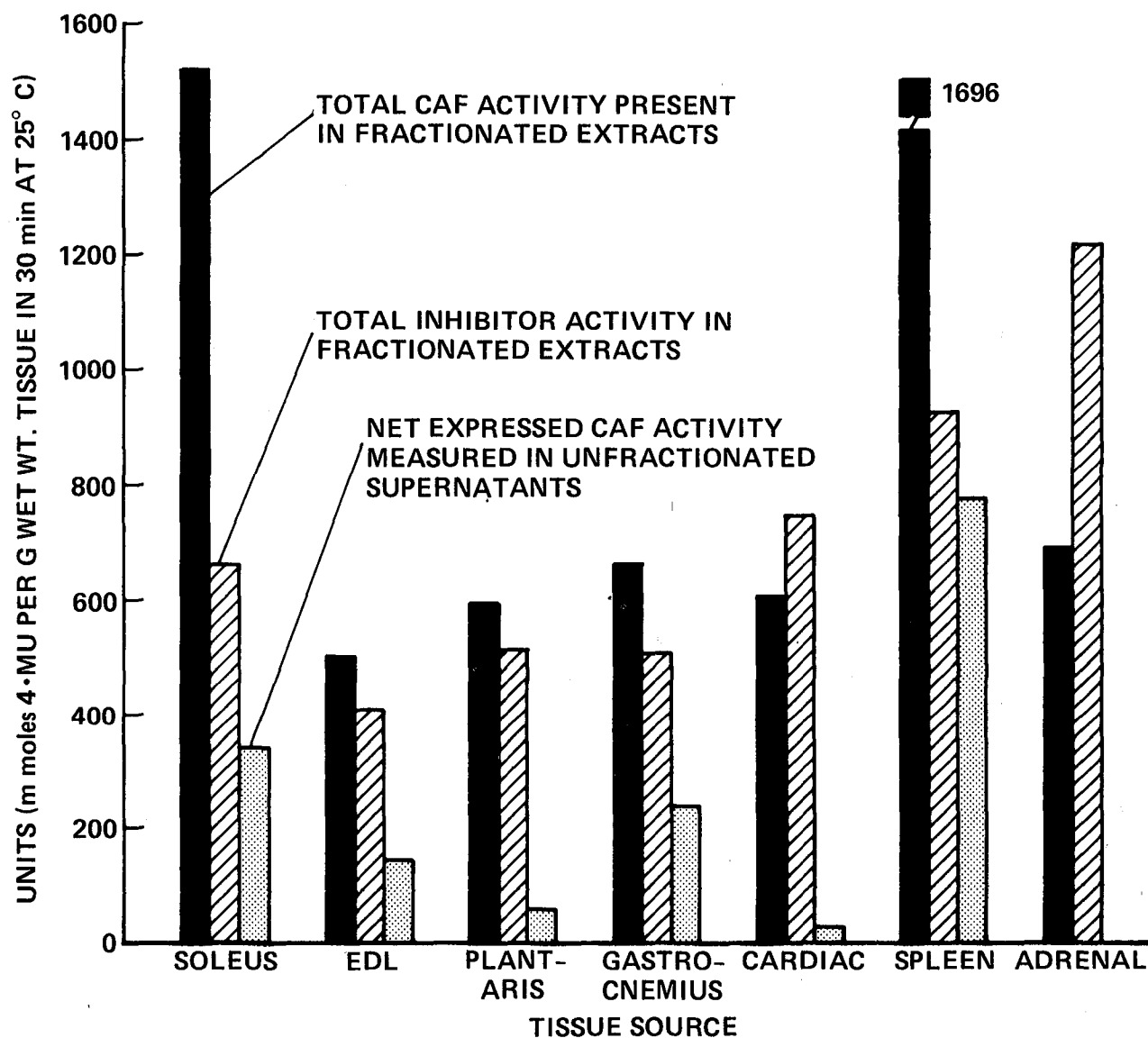


Fig. 20. (Ellis and Nagainis 199-20-42-01)

PROTEOLYSIS IN MUSCLE ATROPHY 199-20-42-01

S. Ellis, Ames Research Center, Biomedical Research Division
P. Nagainis, National Research Council Associate
C.R. Ashmore, University of California, Davis
D.A. Riley, Medical College of Wisconsin

Efforts to define the role of proteases in the development of muscle atrophy centered on a lysosomal protease, tripeptidyl aminopeptidase (TAP), and on a cytosolic protease, Ca^{2+} -activated factor (CAF). Using highly purified bovine liver TAP, anti-sera was prepared in rabbits to prove by immuno-cytochemical techniques at the electron microscope level that TAP is localized in lysosomes, and perhaps even restricted to the lysosomal membrane. With regard to CAF, a highly sensitive assay method was developed based on the hydrolysis of casein tagged with a fluorescent label. This method permits the assay of CAF in muscle samples as small as 50 mg, and was used to discriminate between the CAF isozyme activated by micromolar (as opposed to millimolar) concentrations of Ca^{2+} for full activity. With this method the concentrations of CAF were measured in some muscles of the rat hind limb. The concentrations of CAF in several hind-limb muscles (Fig. 20) was low except for the soleus muscle, which contained a threefold concentration over other muscles. CAF was proposed as the protein which initiates the hydrolysis of proteins constituting the Z-band of myofibrils, thereby affecting the disassembly of the sarcomeres. The high levels of CAF in the soleus muscle were consistent with the higher protein turnover, and also the exceptional sensitivity of this anti-gravity muscle to atrophy from disuse.

In histochemical studies of the distribution of carbonic anhydrase (CA), the dorsal root ganglia contained sub-populations of sensory neurons with moderate to high CA activity, whereas in the ventral root of the reactive neurons, CA was in the gamma motor range. With this technique, studies will attempt to correlate the atrophy of muscle with atrophy of innervation.

Publications: none

GROWTH FACTORS AND MUSCLE ATROPHY 199-20-42-02

S. Ellis, Ames Research Center, Biomedical Research Division
C.R. Ashmore, University of California, Davis

Research concentrated on the hypothesis that growth factors, intrinsic to muscle, stimulate muscle cells when the muscle is subjected to loading, activity, or stretch. Stretched chicken muscle appeared to contain increased amounts of a mitogenic substance which stimulates precursor cells of striated muscle to grow and proliferate, and to synthesize the enzyme creatine phosphokinase, which is typical of adult muscle. When chicken muscle was released from stretch, the concentration of intrinsic growth factor returned to control levels. The factor appeared to be a protein. Efforts were started to test this reaction in rat muscle, and to establish the nature of the growth factor. Findings were consistent with the concept that intrinsic growth factors were expressed within stretched muscle, which serves to stimulate protein synthesis, myoblast proliferation, and fusion.

Publications: Riley, D.A., and S. Ellis. 1983. "Research on the adaptation of skeletal muscle to hypogravity: Past and future directions." ADVANCES IN SPACE RESEARCH 3: 191-197.

THE ROLE OF BIOASSAYABLE GROWTH HORMONE IN PROTEIN BALANCE 199-20-42-03

R.E. Grindeland, Ames Research Center, Biomedical Research Division
M. R. Heinrich, Ames Research Center, Biosystems Division
W. Hymer, Pennsylvania State University, University Park, PA

Growth hormone-secreting cells (somatotrophs) from rat pituitary glands, separated into two types by a density gradient, were put into Amicon hollow fibers and implanted into hypophysectomized rats. In response to Type 1 somatotrophs, body and muscle weights held their own, whereas a mixture of the two types of pituitary cells resulted in small gains. Type 2 somatotrophs significantly increased body and muscle weights compared to those of rats implanted with empty capsules.

Synthetic growth hormone releasing factor (GRF) enhanced bone growth in intact rats; immunoreactive growth hormone (IR-GH) was not detectable in plasma of implanted rats and appeared in very low levels in GRF treated rats, indicating that the growth was mediated by bioassayable growth hormone (BA-GH). Isolation of Type 1 and 2 somatotrophs was improved by use of percoll, rather than by serum albumin gradients.

Free flow electrophoresis also achieved significant separation of the two cell types, and was especially effective in weightlessness during Space Shuttle flight (STS-8). One electrophoretic fraction containing Type 1 somatotrophs was enriched about three times greater than fractions achieved by a density gradient on Earth. Type 2 cells showed a concentration essentially the same as that from density gradients on Earth. The results clearly showed that the two cell types differ not only in histology and density, but in electrical charge. On the other hand in the microgravity environment on STS-8, mixtures of pituitary cells in two different buffers secreted significantly less growth hormone than cells maintained on Earth, suggesting that weightlessness caused a secretory lesion.

Publications: Grindeland, R.E. 1982. "Space weightlessness and hormonal changes in human subjects and experimental animals." in Space Gerontology (NASA Conference Publication 2248). Moffett Field, CA: Ames Research Center. pp. 55-57.

MITOCHONDRIAL FUNCTION IN DISUSE-ATROPHIED SKELETAL MUSCLE 199-20-42-05

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S. Ellis, Ames Technical Monitor

After seven to 14 days of cast immobilization of rat hind limbs (50% muscle weight loss) the oxidative enzymes of the Krebs cycle (citrate synthase) and of fatty acid oxidation (3-hydroxy-acyl-CoA dehydrogenase) were reduced by 20% in both high-oxidative, fast-twitch gastrocnemius-plantaris muscles, and high-oxidative, slow-twitch soleus muscles. Reductions in oxidative enzymes enhanced fatigue and glycogen depletion of atrophied muscle. The

tension output of the casted muscles decreased 45% with a 7% to 10% loss in relative tension throughout the fatigue test, and a 17% glycogen loss. (This task was successfully completed and terminated.)

Publications: none

GONADAL STEROIDS AND MUSCLE ATROPHY 199-20-42-06

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S. Ellis, Ames Technical Monitor

Much of the past year's effort focused on modes of regulation of androgen receptors in muscle. This focus was due to the key function of the receptor as a determinant of androgen action on muscle, and hence, as a crucial factor in regulation of muscle mass and function. Orchiectomy caused a striking increase in androgen receptor binding by the tibialis anterior and extensor digitorum longus muscles. This effect was blocked by cycloheximide and may reflect de novo receptor synthesis. Thus androgen seemed to down-regulate its own receptor in muscle.

In another study, a single injection (100 g) of estradiol-17 caused a twofold increase in the number of cytosolic androgen receptors in rat levator ani muscle. Dose-response studies revealed this effect with 10 g of estradiol. This phenomenon supported our hypothesis of androgen/estrogen synergy in muscle, and it may reveal an important mode of regulation of muscle mass and function. Future work will study skeletal muscle.

In another study, denervation of rat skeletal muscle caused a transient 50% increase of cytosolic androgen receptor number. This effect was mimicked by subperineurial injection of tetrodotoxin, which causes pure disuse of skeletal muscle. This effect apparently did not require de novo receptor synthesis; rather it may involve transfer of nuclear receptors to the cytoplasm. Thus, muscle disuse had an effect on receptor binding. (The significance of this effect to maintenance of muscle mass and function requires further work.) These data revealed a number of important regulatory mechanisms of muscle hormone sensitivity. They concerned skeletal muscle as well as hormone-dependent muscle, and they should provide insight into mechanisms of muscle atrophy as well as possible therapeutic and preventive strategies.

Publications: (1) DuPois, D.C., and S.R. Max. 1983. "Effect of denervation and reinnervation on oxidation of glucose 6-¹⁴C on rat skeletal muscle homogenates." JOURNAL OF NEUROCHEMISTRY 40: 727-733. (2) Hall-Craggs, E.C.B., S.R. Max, M.M. Wines, T.M. Moreland, and J.R. Hebel. 1983. "Central core degeneration following tenotomy in soleus muscles of hyperthyroid rats." EXPERIMENTAL NEUROLOGY 81: 722-732. (3) Hall-Craggs, E.C.B., M.M. Wines, and S.R. Max. 1983. "Fiber type changes in denervated soleus muscles of the hyperthyroid rat." EXPERIMENTAL NEUROLOGY 80: 252-253. (4) Max, S.R. 1983. "Cytosolic and androgen receptor in skeletal muscle from normal and dystrophic mice." JOURNAL OF STEROID BIOCHEMISTRY 18: 281-283. (5) Max, S.R., and G.J. Markelonis. 1983. "Neuromuscular interactions." NEUROCHEMISTRY INTERNATIONAL 5: 675-683. (6) Max, S.R., and J. Toop. 1983. "Androgens enhance 2-deoxyglucose uptake by rat levator ani

muscle in vivo." ENDOCRINOLOGY 113: 119-126. (7) Yeagle, S.P., R.F. Mayer, and S.R. Max. 1983. "Contractile properties of fast-twitch skeletal muscle of normal, testosterone-treated and castrated rats during reinnervation." EXPERIMENTAL NEUROLOGY 82: 344-357.

MUSCLE FIBER TYPE DISTRIBUTION RELATIVE TO MUSCLE WEAKNESS: A NEW METHOD
190-20-42-07

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S. Ellis, Ames Technical Monitor

The distribution of muscle fiber types in the male monkey Macaca mulatta was determined by the differential ratio of strontium and calcium ions ($\text{Sr}^{2+}/\text{Ca}^{2+}$) that activates muscle tension. Fast-twitch fiber required twice as much Sr^{2+} as slow-twitch fiber. The percentage of fast/slow fibers in some primate muscles were as follows: vastus lateralis, 94/6, soleus 24/76, plantaris 84/16, superficial masseter 13/84, temporalis 22/78.

Publications: none

MECHANISM AND CONTROL OF DISUSE ATROPHY IN SKELETAL MUSCLE 199-20-42-10

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We previously demonstrated that leupeptin- and E-64-C-sensitive non-lysosomal proteases were responsible for elevated proteolysis induced by calcium ionophores and other agents. During the past year, a second distinct role for calcium in regulating lysosomal proteolysis was discovered. Calcium ionophores and other agents affecting calcium movement prevented the elevation of proteolysis caused by removal of serum factors like insulin, leucine, or Multiplication Stimulating Activity (MSA) from the incubation medium. The calcium dependency of lysosomal proteolysis seemed to involve calmodulin, because known calmodulin inhibitors like trifluoperazine (TFP), an anti-psychotic drug, can selectively block enhanced (stepdown) proteolysis seen in the absence of serum factors. In contrast, calmodulin inhibitors did not block the enhanced non-lysosomal calcium-dependent proteolysis. TFP was also found to be effective in retarding muscle atrophy as well as promoting net muscle growth in vivo; TFP reduced significantly loss of muscle protein in vitamin E deficient guinea pigs, and in starved, hyperthyroid, and even normal rats. Prostaglandins were recently implicated in calcium- and stretch-dependent regulation of protein metabolism in muscle. Aspirin selectively reduced atrophy of the slow-contracting soleus muscle in the cast-immobilized rat model. These studies suggested that prostaglandins and calcium may be involved in disuse atrophy.

Publications: none

BIOCHEMICAL ADAPTATIONS OF ANTIGRAVITY MUSCLE FIBERS TO DISUSE ATROPHY 199-20-42-12

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S. Ellis, Ames Technical Monitor

Research continued into the molecular basis of the immobilization-induced decrease in muscle size. Rat hind limbs were held rigid in plaster of Paris. We observed that the content of α -actin mRNA was unchanged when actin synthesis was decreased in muscles immobilized for six hours. This observation suggested that the defect in the actin synthetic pathway was translational. A hormonal signal initiating the decrease in muscle protein synthesis could not be demonstrated. No difference in the numbers of specific dexamethasone-binding sites was observed in the cytosol of muscles from control rats and from limbs immobilized for six hours. Whereas protein synthesis rate decreased, and insulin-stimulated 2-deoxyglucose uptake decreased in muscles from the immobilized hind limb, these values were normal in muscles from the contralateral, non-immobilized limb of the same rat. Our previous observation of insulin resistance for 2-deoxyglucose uptake in muscles of immobilized limbs was not related to a decrease in the number of insulin receptors, but was likely caused by a post-receptor defect. Our previous report of insulin resistance for glycogen synthesis in immobilized muscle was likely a result of at least two factors: an inability of insulin to supply sufficient glucose for glycogen synthesis, and a decreased ability of insulin to activate glycogen synthase.

Publications: (1) Booth, F.W., and P.D. Gollnick. 1983. "Effects of disuse on the structure and function of skeletal muscle." MEDICINE AND SCIENCE IN SPORTS AND EXERCISE 15: 415-420. (2) Watson, P.A., A. Srivastava, and F.W. Booth. 1982. "Cytochrome C synthesis rate is decreased in the sixth hour of hind limb immobilization in the rat." in Biochemistry of Exercise, International Series on Sport Sciences Vol. 13. Human Kinetics Publishers: Champaign, IL. 378-384.

ALTERATIONS IN SKELETAL MUSCLE WITH DISUSE ATROPHY 199-20-42-13

R.E. Fitts, Marquette University, Milwaukee, WI, Department of Biology
S. Ellis, Ames Technical Monitor

Cast immobilization of the rat hind limb for six weeks in the shortest possible position produced a shorter soleus muscle, reduced fiber length, no change in sarcomere length, but a 27% reduction in sarcomere number per fiber. This probably accounts for the reduced extensibility observed after immobilization. Twitch duration times (CT + 1/2RT) for the soleus muscle dropped precipitously during the four-day period after casting by 23% below the precast level. On the other hand, the EDL (extensor digitorum longus muscle, 60% fast twitch) and the SVL (superficial vastus lateralis muscle, 100% fast twitch) showed a significant increase in twitch duration. After seven days of immobilization the new values stayed constant for the duration of immobilization (42 days). Studies on recovery from six weeks of immobilization showed that isometric twitch duration of the shortened soleus returned to normal after four days for contraction time and seven days for half-relaxation time. Immobilization for six weeks produced a 60% decline

in the Ca^{2+} uptake rate of vesicles of the sarcoplasmic reticulum from the slow soleus muscle, a doubling in the case of the fast SVL, and no change in the fast type IIA deep in the vastus lateralis muscle.

Publications: Witzmann, F.A., D.H. Kim, and R.H. Fitts. 1983. "Effect of hindlimb immobilization on the fatigability of skeletal muscle." JOURNAL OF APPLIED PHYSIOLOGY 54: 1242-1248.

IMMOBILIZATION/RE-IMMOBILIZATION AND THE REGULATION OF MUSCLE MASS 199-20-42-14

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Molecular Biology

S. Ellis, Ames Technical Monitor

Researchers delineated the changes in size of both the soleus and EDL muscles as a function of animals in the weight range of 50 to 120 g. They also developed baseline data for the following parameters: total protein, total non-collagen protein, total collagen, soluble protein, total myofibrillar protein, myofibrillar non-collagen protein, collagen in the myofibrillar fraction, and DNA content. They developed a casting technique, using plastic (Scotchcast) tape, only 1/10 the weight of plaster casts, which can be used on mice as well as rats, and permits free movement of the animal during immobilization of a limb.

Publications: none

FLUID AND ELECTROLYTE CHANGES

Fluids are redistributed in the body during weightlessness. More blood shifts to the head and thorax during spaceflight, instead of pooling in the lower limbs as under the effects of normal gravity. Facial puffiness and nasal congestion accompany fluid shifts. Investigators were first able to study these effects on astronauts during the lengthy missions of Skylab in the early 1970s.

Apparently this headward shift of fluids alters the level of hormones in the blood from the cortex (outer region) of the adrenal gland, changing the homeostatic control that balances salts and water in the body. Because fluid-retaining hormones decrease, blood volume decreases. During bedrest to simulate the effects of weightlessness, the circulating level of these hormones decreases for 24 hours and then adapts to a new, stable level. The resulting reduction of fluid volume provides a lower than normal blood flow to the head under the +Gz forces similar to those experienced during reentry of the Space Shuttle. Hormonal changes also trigger an excretion of sodium (Na) and, to a lesser extent, potassium (K), along with water. Salt losses continue for the duration of bedrest studies, as the body eliminates more salt than it takes in. These fluid and hormonal shifts may also affect metabolism relating to motion sickness, muscle atrophy and bone loss.

This RTOP investigates changes of the hormones in urine and plasma that regulate the excretion and reabsorption of salt and water from the kidney. These hormones include:

- o glucocorticoids such as cortisol, which maintains blood volume and pressure in the body, produced in the adrenal cortex;
- o mineralocorticoids such as aldosterone, which controls sodium levels in the body, produced in the adrenal cortex;
- o arginine vasopressin, the anti-diuretic hormone (ADH), which maintains fluid volume in the body, produced in the pituitary;
- o a natriuretic hormone, a recently discovered protein (hormone), which causes sodium excretion in the urine.

Basic research at Ames focuses on a variety of studies with animals and studies with humans, who are subjected to bedrest in a gentle, head-down (-6°) position to simulate the hemodynamic effects of weightlessness. Information and expertise derived from these bedrest studies also contributes to NASA's program in Operational Medicine (see pp. 13 and 21).

HORMONE MECHANISMS REGULATING FLUID AND ELECTROLYTE METABOLISM IN WEIGHTLESSNESS AND BEDREST 199-20-62-01

J. Vernikos-Danellis, Ames Research Center, Biomedical Research Division

Research continued into the nature of the hormonal systems regulating the body's fluid and electrolyte balance during bedrest and in response to a standard posture test (SPT), a test of orthostatic tolerance (susceptibility to fainting) when the subject stands up after one hour of lying down. Two similar studies were conducted previously with male subjects aged 35 to 50. In this year's study, eight women, aged 30 to 45 (Fig. 21) were tested for the effects of weightlessness on body fluids. Weightlessness was simulated by seven days of bedrest with the head lowered 6° from the horizontal (-6°). Although women of different ages were tested previously in horizontal (0°) bedrest, this study marked the first time women were tested in the -6° head-down position, which mimics more effectively the pronounced fluid and electrolyte changes that occur in 0 G.

After preliminary screening, which included a determination of plasma volume, cardiovascular and hormone responses to a SPT, and taking into consideration the phase of their menstrual cycles, eight subjects were selected from a pool of 16 volunteers. The study was designed so that bedrest occurred during the second or third week of their menstrual cycles. Subjects were selected to cover the widest possible range of normal blood pressures and plasma volumes so that a fair assessment of the contribution of their initial physiological status to their post-bedrest orthostatic tolerance could be made.

Preliminary data showed that women react to the -6° head-down position similarly to men. Hormone mechanisms that regulate fluid retention and stimulate the circulation were suppressed within the first 30 minutes in the head-down position, causing more fluid to be eliminated from the body. These hormones continued at a decreased level for 24 hours, when they returned to a new, normal, adaptive level. Although excessive fluid loss was only apparent for the first 24 hours, loss of sodium (Na) continued for the duration of the bedrest. The response of female subjects was not significantly different from males tested previously under identical conditions.

The response of the rush of blood to the head during the first 24 hours head down was a mirror image of the body's response to the rush of blood to the feet each time a person stands up. Standing up after just one hour of lying down brought about an increase in heart rate, a decrease in blood volume and an increase in the levels of hormones (antidiuretic hormone, angiotensin, aldosterone, cortisol, norepinephrine), whose ultimate function are the retention of fluids and the stimulation of the circulation. The response to standing up after seven days of head-down bedrest was merely an amplification of this normal and necessary body response.

Apparently, an amplification of the endocrine response to an orthostatic challenge is essential to compensate for the fluid and vascular changes of head-down bedrest. If, for any reason (initial physiological status or deliberate down-regulation of these systems), one or more of the body's



Fig. 21. Eight women involved in a bedrest study to determine the effects of simulated weightlessness on females aged 30 to 45. Left to right, back row: Kay Holley, Linda Willis, Janice Walden, Consuelo Bennett; front row: Carol Yanz, Karen Kettlety, Lynn Hinds, Candace Eng. (Vernikos-Danellis 199-20-62-06)

regulatory neurohumoral systems do not show an adaptive, amplified response to standing, then the probability of post-bedrest orthostatic intolerance, or fainting, is greatly increased.

Publications: Vernikos, J. 1984. "Stress response as a function of age and sex." in Breakdown in Human Adaptation to Stress, Vol.1, Pt.2. Wegmann, H.M., ed. Boston, MA: Kluwer Academic. p. 509.

CENTRAL NERVOUS SYSTEM MECHANISMS AFFECTING SALT/WATER BALANCE 199-20-62-02

L.C. Keil, Ames Research Center, Biomedical Research Division

In the rat, vasopressin (the anti-diuretic hormone secreted from the pituitary) was found to be regulated by endogenous opioid peptides, morphine-like in action. This finding may explain why vasopressin secretion is modified during periods of pain and stress. Vasopressin also inhibited the secretion of renin from the kidney, which could explain the elevated renin levels when vasopressin levels are low during bedrest and spaceflight.

Another study showed that an inflatable aviator's suit, the anti-G suit, may be useful in studying the acute hormonal response during headward fluid shift, which is common during weightlessness in spaceflight. Inflated around a pilot's lower body, air pressure forces fluids headward. This process maintains blood pressure to the pilot's head during high speed turns and prevents blackout and greyout. Unlike water immersion, use of the anti-G suit allows blood sampling and blood pressure measurements without movement by the subject, and avoids possible infections that may develop around the venapuncture site in water.

Publications: (1) Billman, G.E., M.J. Keyl, D.T. Dickey, D.C. Kem, L.C. Keil, and H.L. Stone. 1983. "Hormonal and renal response to plasma volume expansion in the primate *Macaca mulatta*." AMERICAN JOURNAL OF PHYSIOLOGY 244: H201-H205. (2) Convertino, V.A., L.C. Keil, and J.E. Greenleaf. 1983. "Plasma volume, renin and vasopressin responses to graded exercise after training." JOURNAL OF APPLIED PHYSIOLOGY 54: 508-514. (3) Jerome, M.L., Y.R. Barbella, J. Wurpel, L.C. Keil, and W.B. Severs. 1983. "Eating, drinking and urine output after prolonged cerebroventricular vasopressin infusions in rats." PHARMACOLOGY 26: 79-84. (4) Keller-Wood, M.E., C.E. Wade, J. Shinsako, L.C. Keil, G.R. Van Loon, and M.F. Dallman. 1983. "Insulin-induced hypoglycemia in conscious dogs: Effect of maintaining carotid arterial glucose levels on the adrenocorticotropin, epinephrine, and vasopressin responses." ENDOCRINOLOGY 112: 624-632. (5) Raff, H., J. Shinsako, L.C. Keil, and M.F. Dallman. 1983. "Vasopressin, ACTH and corticosteroids during hypercapnia and graded hypoxia in dogs." AMERICAN JOURNAL OF PHYSIOLOGY 244: E453-E458. (6) Schwartz, J., L.C. Keil, J. Maselli, and I.A. Reid. 1983. "Role of vasopressin in blood pressure regulation during adrenal insufficiency." ENDOCRINOLOGY 112: 234-238.

**FLUID AND ELECTROLYTE SHIFTS DURING IMMERSION: METABOLISM, WORK
PERFORMANCE AND ACCELERATION TOLERANCE 199-20-62-06**

J.E. Greenleaf, Ames Research Center, Biomedical Research Division

Studies with S.E. Kravik, National Research Council Associate from Ullevaal Hospital in Norway, expanded the usefulness of the inflatable aviator's suit, or anti-G suit, for basic research in space medicine (Fig.22). At NASA's Ames Research Center, Ullevaal Hospital and other medical research centers, experiments had been conducted using a clinical version of the anti-G suit, which can dramatically stop serious abdominal bleeding (following childbirth or pelvic fracture) within 30 seconds with a suit pressure of 20 mmHg.

To cause a headward shift of fluids similar to that produced by immersion in water, the suit is inflated to apply lower body positive pressure (LBPP). LBPP appears promising as an adjunct to immersion for studying fluid and electrolyte shifts and associated hormonal responses. As a simulation for some of the effects encountered during spaceflight, LBPP eliminates the artificial effect of water pressure on the body during immersion.

In other research studies, G. Geelen, a European Space Agency fellow, found that rapid drinking of tap water significantly inhibited plasma vasopressin



Fig. 22. Subject wearing an anti-G suit during a controlled study of fluid shifts and hormone changes, similar to those encountered in spaceflight. (Greenleaf 199-20-62-06)

(PVP) in dehydrated humans. Previously attributed to an increase in right atrial pressure during immersion, PVP suppression was also noted in subjects who drank water during immersion. V.A. Convertino observed no change in tilt-table (orthostatic) tolerance in subjects after a total of 16 hours of exercise training, in spite of a significant increase in maximal oxygen uptake of 8.3%. Whether a much longer period of exercise training is necessary to determine if training significantly lowers orthostatic tolerance remains unknown. N. Wong concluded that isotonic and isometric arm exercise performed concurrently with leg exercise causes significant errors in measures of glucose and lactic acid concentrations in venous blood samples taken from the arm. W.A. Spaul studied the effects on thermoregulatory responses of vibration on the whole body and the arm. Vibration significantly depressed sweating. Whole body vibration may be responsible for the increased number of heat casualties among desert troops during and after riding in vehicles. M.H. Harrison completed preliminary studies on the effects of dehydration and hyperhydration on fluid, electrolyte and protein shifts during head-up tilting, and began analysis of the data.

Publications: (1) Convertino, V.A., L.C. Keil, and J.E. Greenleaf. 1983. "Plasma volume, renin, and vasopressin responses to graded exercise after training." JOURNAL OF APPLIED PHYSIOLOGY 54: 508-514. (2) Fregly, M.J., N.E. Rowland, and J.E. Greenleaf. 1983. "Effects of yohimbine and tolazoline on isoproterenol and angiotensin II-induced water intake in rats." BRAIN RESEARCH BULLETIN 10: 121-126. (3) Geelen, G., L.C. Keil, S.E. Kravik, C.E. Wade, T.N. Thrasher, P.R. Barnes, G. Pyka, C. Nesvig, and J.E. Greenleaf. 1983. "The effect of drinking on plasma vasopressin and renin in dehydrated human subjects." in Space Physiology. Garcia, J., M. Guerin, and C. Laverlocher, eds. Toulouse, France: Cepadues Editions, pp. 427-429. (4) Greenleaf, J.E. 1983. Bedrest Studies: Fluid and Electrolyte Responses (NASA Technical Memorandum 84357). Moffett Field, CA: Ames Research Center, 17 p. (5) Greenleaf, J.E. 1983. "Bed-rest studies: fluid and electrolyte responses." in Space Physiology. Garcia, J., M. Guerin, and C. Laverlocher, eds. Toulouse, France: Cepadues Editions, pp. 335-348. (6) Greenleaf, J.E., P.J. Brock, L.C. Keil, and J.T. Morse. 1983. "Drinking and water balance during exercise and heat acclimation." JOURNAL OF APPLIED PHYSIOLOGY 54: 414-419. (7) Greenleaf, J.E., J.T. Morse, P.R. Barnes, J. Silver, and L.C. Keil. 1983. "Hypervolemia and plasma vasopressin response during water immersion in men." JOURNAL OF APPLIED PHYSIOLOGY 55: 1688-1693. (8) Greenleaf, J.E., W. Van Beaumont, V.A. Convertino, and J.C. Starr. 1983. "Handgrip and general muscular strength and endurance during prolonged bedrest with isometric and isotonic leg exercise training." AVIATION, SPACE AND ENVIRONMENTAL MEDICINE 54: 696-700. (9) Kikta, D.C., C.C. Barney, R.M. Threatte, M.J. Fregly, N.E. Rowland, and J.E. Greenleaf. 1983. "On the mechanism of serotonin-induced dipsogenesis in the rat." PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR 19: 519-525.

BIOLOGICAL EFFECTS OF PARTICLE RADIATION

Ionizing radiation in space, including electrons, protons, neutrons, x-rays, and galactic cosmic rays, represents a potential danger to the health of astronauts and their performance during flight operations. The long-term effects from low doses of heavy, high-energy (HZE) particles, such as carbon, iron and argon, have never been studied extensively. Experimental studies of radiation effects by the scientific community in the past primarily focused on the problem of the short-term effects of a large, single exposure to radiation. With Shuttle astronauts in orbit at more frequent intervals, and future operations at higher orbits for long periods of time, the risk of long-term effects from radiation is significant. Radiation levels also increase in high inclination orbits, such as the polar orbits planned for Space Shuttles launched from the Western Test Range at Vandenberg AFB. A solar flare in 1972 would have exposed an astronaut in polar orbit to 200 rads. NASA's limits for radiation exposure to the eyes are currently 0.3 rad. The average exposure on the Shuttle in low earth orbit is 5 to 6 millirems per day, with 27 millirems recorded during the complete STS-5 mission.

Research under this RTOP includes determining both short- and long-term effects of HZE particles on cells and organs, including the possible risk of cancer. The threshold exposure from radiation is studied, above which deleterious biological effects are expressed, especially affecting the aging and mortality of neural and retinal tissue. The effects of multiple exposures of biological tissue to radiation is also investigated.

L.M. Kraft, Ames Research Center, Biomedical Research Division
W.L. Savage, San Jose State University, Department of Biological Sciences

Studies continued on the reduction in life span due to lethal tumors in mice exposed to heavy, high energy (HZE) particle radiation in the BEVALAC at the University of California, Berkeley. Preliminary results with regard to neon (^{20}Ne) particle radiation were added to the previous report, which dealt only with carbon (^{12}C) particles and γ -rays (^{60}Co). Estimated relative biological effectiveness (RBE) was calculated. When the values were compared with those for carbon particles, the RBE was less for neon at two LET (linear energy transfer) values than for carbon (Fig. 23). Additional data are currently being obtained from mice irradiated with silicon, argon, and iron particles.

ESTIMATED RELATIVE BIOLOGICAL EFFECTIVENESS (RBE) OF HZE PARTICLES AT VARIOUS LINEAR ENERGY TRANSFER (LET) VALUES AT 10% LIFE SHORTENING DUE TO LETHAL TUMORS IN MICE

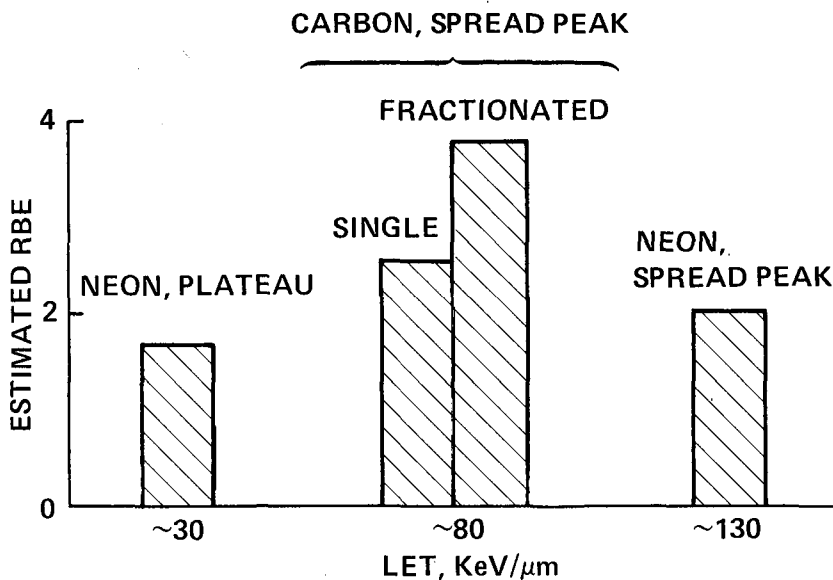


Fig. 23. Carbon particle radiation as both single and fractionated doses resulted in apparently greater life shortening in mice than neon particle radiation delivered at the indicated LET values. The total fractionated dose is the same as a single dose, but delivered into 24 equal weekly fractions. (LET: linear energy transfer) (Kraft 199-20-72-08)

A Zeiss IBAS I and II image analyzer has been installed and is operational. Its capabilities are extensive and its operation greatly simplified (user friendly) by means of software packages, both standard and optional. This equipment will be useful in studies additional to those for which it was acquired.

Publications: (1) Kraft, L.M., K. Joyce, and E.D. D'Amelio. 1983. "Removal of histological sections from glass for electron microscopy: Use of Quetol 651 resin and heat." STAIN TECHNOLOGY 58: 41-43. (2) Kraft, L.M. 1983. "Genetic engineering and the laboratory animal." CHARLES RIVER DIGEST 22(2).

EFFECTS OF PARTICLE RADIATION ON THE AGING RETINA AND BRAIN 199-20-72-11

D.E. Philpott, Ames Research Center, Biomedical Research Division

Both the retina and brain of mice were studied after exposure to low radiation doses and examination of the animals was made over a long period of time. At the Lawrence Berkeley Laboratory 42 mice were irradiated: half at 0.5 rad and the other half at 50 rads. A control group of 21 mice were maintained for comparison. Groups were sacrificed at three, six, and 12 months after irradiation. Results showed an increase in age pigment resulting from destruction of the mitochondria in tissue cells (Fig. 24), accompanying a decrease in performance ability (longer time and more errors when running a maze, and loss of neuromotor ability when walking a tightrope).

Work continued on counting the populations of individual cells following irradiation of the testes. Counts of cell populations resulted in predicted survival curves. Previous work resulted in abnormal survival curves. Use of linear regression produced a straight line, masking the response of the different cell types. Thus, results must be plotted for the individual cell populations before linear regression can be used to calculate the percentage of cell deaths resulting from a specific dose of radiation.

A radiation meeting was also organized for the Scanning Electron Microscope meeting in Detroit, bringing a major focus on low dose, long-term radiation effects from HZE particles to help encourage scientific interest in the review of the maximum safe exposure for space passengers and crews.

Publications: (1) Philpott, D., W. Sapp, C. Williams, J. Stevenson, R. Corbett, and S. Black. 1983. "Response of the seminiferous epithelium of the mouse exposed to low dose high energy (HZE) electromagnetic radiation." SCANNING ELECTRON MICROSCOPY Chicago, IL: SEM Inc. pp. 1345-1351. (2) Philpott, D. 1983. "Ultrastructural effects of radiation on tissues and cells: An overview." in Ultrastructural Effects of Radiation on Tissues and Cells, Chicago, IL: Scanning Electron Microscopy, Inc. iii. (3) Philpott, D.E., W. Sapp, C. Williams, J. Stevenson, S. Black, and R. Corbett. 1983. "The response of a mixed cell population in mouse testes to x-ray and HZE irradiation." PROCEEDINGS OF THE ELECTRON MICROSCOPE SOCIETY OF AMERICA 41: 674-675.

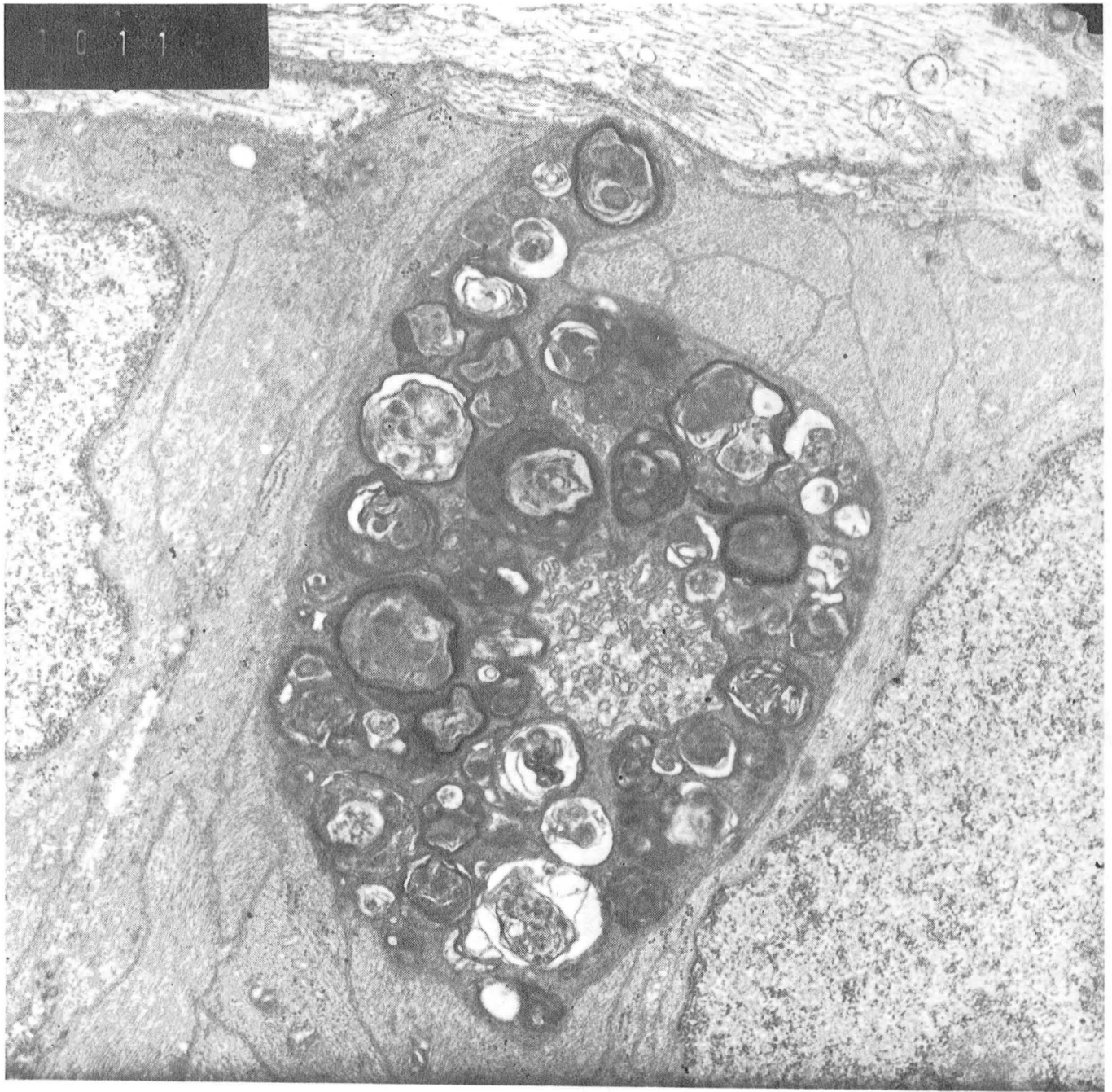


Fig. 24. Deterioration in the retina cell from a mouse at six months after irradiation with 50 rads of Argon particles. Age pigment and debris in a neuron (dark-stained area in center of micrograph) of the outer nuclear layer in the retina magnified 27,500x. (Philpott 199-20-72-11)

Manned space missions require high levels of human performance in unfamiliar and stressful environments. Future missions will involve career astronauts, scientist passengers chosen for their technical expertise, and ultimately members of the population at large. Because of the high cost of the Space Shuttle missions, their short duration, and the high value of their successful completion, every effort must be made to maximize the successful performance and adjustment to mission conditions by all crew members and passengers. The space environment presents a unique blend of behavior and performance stresses, both psychological (confined space, heavy workload, short flight time) and physiological (weightlessness followed by reentry accelerations).

The psychological effects on behavior include flight procedures and situations that can either lead to effective or ineffective performance by the individual or group. Habitation in flight among people of different nationality, personality and gender will become commonplace in the Shuttle era. Studying crew composition and hierarchical or cooperative structures can achieve the best possible mode for successful flight performance; marginal performance by crew members could result in mission failure.

Decrements in behavior and performance can also come from changes in physiology. Body functions can stray from their normal, synchronized rhythms through changes in light-dark cycles and social interaction, and changes in routine, such as work shifts and meal times. Desynchronosis of circadian rhythms may affect performance of Shuttle passengers and pilots in the safe and successful accomplishment of their tasks.

This RTOP, covering the behavioral effects of spaceflight, was transferred to NASA's Space Human Factors Office managed by T.A. Tanner of the Man-vehicle Systems Research Division at Ames. That Division is dedicated to research in the interactions between human behavior and machine systems. The Biomedical Research Division will continue to investigate the effects of weightlessness on the physiological basis of behavior and performance in humans.

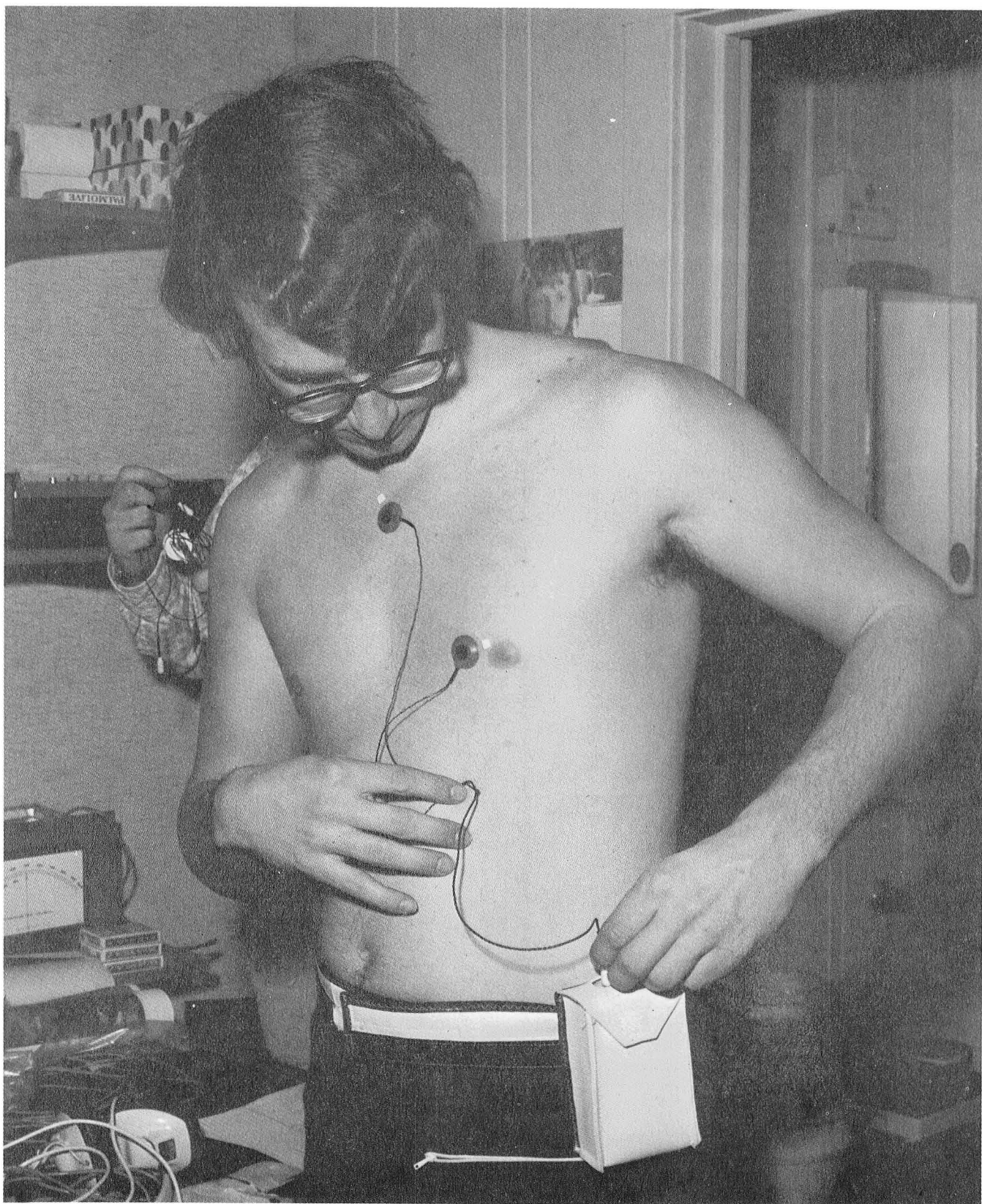


Fig. 25. Subject attaching ECG electrodes to a Biobelt telemetry unit for monitoring circadian rhythms of body temperature and locomotor activity. (Winget 199-20-82-01)

HUMAN BIORHYTHMS: PERFORMANCE AND PHYSIOLOGICAL DECONDITIONING IN WEIGHTLESSNESS 199-20-82-01

C.M. Winget, Ames Research Center, Biomedical Research Division

Recent analyses were completed of experiments in which male human subjects were studied in two groups of three members for 105 days to evaluate the long-term effects of isolation and absence of environmental synchronizers upon adaptability to a simulated Shuttle environment. During constant light regimens, subject triads demonstrated mutual synchronization of their daily rhythms. When a new member was introduced into a subject triad group, social influences within the group resulted in a change of the period length of the newcomer's daily rhythm in constant light. One individual who deviated from other members of an isolated triad in several physiological and psychological parameters exhibited impaired capacity to synchronize his daily rhythms with the other group members. These results emphasize the importance of individual factors in determining adaptability to small isolated groups in a simulated Space Shuttle environment and may be useful in establishing crew selection criteria for future long-term Shuttle (or space station) missions.

Multiple physiological measurements (Fig.25) and a self assessment of arousal were made in eight men on the first, third and fifth days of bedrest. Additional measurements of memory and dexterity task performance were made on the third day. Although none of the individual physiological variables predicted subsequent performance, an alertness factor comprised of certain physiological measures and arousal was a good predictor of subsequent performance. The individual patterns of correlations between variables increased on the performance day, indicating an increase in behavioral activation elicited by the performance tasks. This study indicates that measurement of a selected combination of physiological variables may be useful in predicting subsequent performance in future missions.

Publications: (1) Winget, C.M., C.W. DeRoshia, D.C. Holley, L.S. Rosenblatt, and N.W. Hetherington. 1983. "Changes in waveform and periodicity of circadian body temperature rhythm following photoperiod alterations." AEROSPACE MEDICAL ASSOCIATION PREPRINTS, pp. 239-240. (2) Natelson, B.H., C. DeRoshia, J. Damus, M.B. Finnegan, and B.E. Levin. 1983. "Relations between visceral and behavioral functions in men at bedrest." PAVLOVIAN JOURNAL OF BIOLOGICAL SCIENCE 18: 161-168.

BEHAVIORAL AND BIOLOGICAL INTERACTIONS WITH SMALL GROUPS IN CONFINED MICROSOCIETIES 199-20-82-02

J.V. Brady, Johns Hopkins University Medical School, Baltimore, MD
R.M. Patton, Ames Technical Monitor

Studies evaluated the biological and behavioral effects of replacing one member of an established three-person group with a new member. A performance-based criterion was used for selection of the member to be replaced after several days of group activity. Hormonal levels, performance

effectiveness, and sleep work cycles were monitored throughout the course of several, 10-day residential studies. Destabilization of wake-sleep cycles and work schedules characterized the individual and group readjustments accompanying such replacements. Changes in testosterone levels were related to shifts in indices of performance effectiveness. Addition of a team task involving more stringent coordinations between the several participants in the study provided a sensitive measure of both individual and group performance degradation under such replacement conditions.

Publications: (1) Brady, J.V. 1983. Human Behavior in Space Environments: A Research Agenda. Baltimore, MD: Johns Hopkins University, 34 p. (2) Rice, B. 1983. "Space-lab encounters." PSYCHOLOGY TODAY 17(6): 50-58

DETERMINANTS OF INDIVIDUAL AND GROUP PERFORMANCE 199-20-82-03

R.L. Helmreich, University of Texas, Austin
R.M. Patton, Ames Technical Monitor

Drawing on research conducted with isolated groups, psychological factors that may influence performance and social adjustment on future space missions were specified. These factors include diminishing rewards, excitement and novelty, continuing isolation and discomfort, missions of increasing complexity with multiple and conflicting goals, more heterogeneous crews, and concurrently increasing concern with work satisfaction and leisure needs. To deal with these issues, it was necessary to define, measure and validate the utility of hypothesized personality traits relating to performance and social adjustment. Investigators specified two broad clusters of traits, developed inventories to assess them, and continued to validate their usefulness in a variety of real-life situations.

A study of mid-career scientists was also completed. Their research eminence was predicted from a combination of the personality measures and demographic factors. The personality measures predicted individual and crew performance in jet transports, using both flight operations and simulator performance as criteria. Self-perceptions of fatigue, health, and mood while flying were clearly linked to the clusters of psychological personality traits linked to performance.

Publications: Helmreich, R.L. 1983. "Applying psychology in outer space: Unfulfilled promises revisited." AMERICAN PSYCHOLOGIST 38: 445-450.

EFFECTS OF CONSUMING VARIOUS FOODS AND NUTRIENTS ON HUMAN PERFORMANCE AND BEHAVIOR 199-20-82-07

R.J. Wurtman, Massachusetts Institute of Technology, Cambridge,
Department of Nutrition and Food Science
R.M. Patton, Ames Technical Monitor

Fiscal year 1983 accomplishments included in task 199-20-92-10 under the General Biomedical Research RTOP, see pg. 117.

GENERAL BIOMEDICAL RESEARCH

A.D. Mandel, manager

The main objective of this Research and Technology Objectives and Plans (RTOP) is to provide a research program to support studies in areas not specifically covered by other RTOPs. Studies currently focus on infectious disease detection, weightlessness effects on the immune system, and nutritional metabolism.

Confinement in the Space Shuttle favors the exchange of microorganisms among crew members. The most common types exchanged are simple respiratory and gastrointestinal infections, although latent infections from viruses can persist in the body for long periods without obvious symptoms. If a virus does develop further, it tends to be severe. Preventative measures developed include assays to rapidly detect infectious disease in astronauts prior to launch. To indicate the presence of infection, such assays measure numbers of lymphocytes, the body's defense cells, or lymphocytes' secretion of interferon, the body's initial chemical defense to prevent viruses from replicating.

Immunologists also use mitogenic compounds to stimulate the immune response of lymphocytes, which then grow into larger blast cells, mature, and undergo cell division, as if in response to a naturally-occurring antigen. Generally, mitogens elicit a reduced response in lymphocytes from the blood of cosmonauts or astronauts after flight on the other hand lymphocytes from rats flown in space for twenty days show a strong blastogenic response against several mitogens.

Weightlessness may interfere with the activity of lymphocytes and other cells by disrupting cellular transport and concentration of biochemical metabolites, disrupting distribution of cellular organelles, or disrupting some forms of cellular differentiation itself, such as the blastogenic activation of leucocytes. In weightlessness a lymphocyte may become spherical, causing lower DNA synthesis in the cell than in healthy, active, normally-flattened lymphocytes. Lymphocyte response is monitored in experiments on Earth with techniques simulating weightlessness in animals, and in flight experiments, for example, treating lymphocyte cultures with mitogens as in the Shuttle-Spacelab 1 experiment of Swiss researcher Augusto Cogoli.

Since the late 1960s nutritional research sponsored by Ames Research Center elucidated the effects of different foods on brain biochemistry. Since then, biochemical evidence revealed that different nutrients will change the amount of various neurotransmitters in the brain, thereby affecting performance. Nutrients were found to alter the synthesis of neurotransmitters, such as serotonin, dopamine, and norepinephrine. The amounts of these transmitters is limited by the amounts of certain amino acids provided by the proteins in food.

Serotonin-producing neurons assist in inducing relaxed sleep, the desire for a balance of types of food, increased motor activity, stimulating smooth muscle contraction, and decreasing sensitivity to pain, although serotonin

is not as strong as opiates. Serotonin is also a potent vasoconstrictor. Animals sleep less when given a substance that blocks serotonin synthesis. After one carbohydrate meal both older and younger human adults did worse on performance tests.

Serotonin is made directly from the dietary protein tryptophan. A meal rich in carbohydrates usually precedes serotonin release from the brain. This increase in serotonin acts as a signal for the body to choose more protein and less carbohydrate at the next meal.

Catecholamines, another biochemical system of neurotransmitters, appears to be evolutionarily very old. High protein meals provide the amino acid tyrosine, the dietary precursor of the catecholamines dopamine and norepinephrine. Both are synthesized in the neuron along a single pathway: from tyrosine to dihydroxy-phenylalanine, or DOPA, to dopamine to norepinephrine. Dopamine helps to regulate the mental activities of memory and emotion, and to coordinate fine muscular movement, such as picking up small objects. Norepinephrine aids alertness, the coordination of body movement and balance, and control of the hypothalamus, which in turn controls hunger, thirst, body temperature, and blood pressure. Copper and vitamin C also appear to be used in the formation of norepinephrine from dopamine. Future research should continue to correlate plasma amino acids with changes in physiological performance.

Prolonged bedrest decreases the body's ability to effectively metabolize glucose. (Following bedrest, subjects' plasma levels of insulin was 200% above normal and glucose was 10% above normal.) Apparently the body's secretion of insulin is not capable of returning plasma glucose to normal levels, and muscle cells are especially insulin resistance. Excess glucose would then be stored in the body as triglycerides, which in high concentrations can clog blood vessels and lead to cardiovascular maladies such as atherosclerosis. Although the exact process causing the insulin resistance is unknown, a low calorie diet prevents excess glucose and triglycerides accumulating in the blood.

DIAGNOSIS OF PRE-CLINICAL VIRAL ILLNESS AND ANTI-VIRAL PROPHYLAXIS 199-20-92-01

J.G. Tilles, University of California Medical School, Irvine
A.D. Mandel, Ames Technical Monitor

A vaccine study tested the most sensitive biological assays developed under this task for their ability to detect the interferon induced during infection with live, attenuated virus. Students lacking a specific antibody were inoculated alternatively with live, attenuated measles, mumps or rubella virus. Some students also acted as uninoculated controls. Several blood samples were collected for interferon levels, cytopathic effect, and 2'-5' oligoadenylate synthetase levels. Three days after injection all antibody producers demonstrated measured interferon levels for two days, followed by no production of interferon for seven to ten days, followed by an increase in viral replication. A cytopathic inhibition effect was noted at four to seven days after immunization. The assay successfully detected diseased students and can be used for detection of infectious disease in astronauts prior to launch. (This task was successfully completed and terminated.)

Publications: none

MECHANISMS OF INSULIN INSENSITIVITY IN MUSCLE 199-20-92-02

C.B. Dolkas, Ames Research Center, Biomedical Research Division
G.M. Reaven, Veteran's Administration Hospital, Palo Alto, CA

In either insulin resistance or many cases of diabetes, glucose is not assimilated into the body efficiently. Previous studies showed that exercise training enhances insulin sensitivity in man and laboratory animals. As such, the development of insulin resistance that occurs spontaneously as rats age from two to four months was prevented when rats exercised voluntarily. We have studied how long this enhanced insulin sensitivity lasts if rats suddenly discontinue their exercise regime. The rate of body weight gained after exercise influenced the retention of residual insulin sensitivity in muscle. Rats which gained weight rapidly lost their enhanced sensitivity to insulin, whereas rats which gained weight at rates equal to control rats retained insulin sensitivity seven days after the end of exercise. Furthermore, bodies with weight gain limited by eating a calorically reduced diet maintained sensitivity to insulin in both control and retired exercise-trained rats.

Two non-invasive techniques have been under study. A computer model to simulate a glucose tolerance test, and eventually simulating insulin resistance or weightlessness, in humans is being developed. Likewise, an initial study using nuclear magnetic resonance (NMR) imaging and spectroscopy has been done with disused muscles of rats prior to design of studies with humans. NMR whole body scanning could be used in studies with bedrest subjects, or studies with interested astronauts pre- and postflight at convenient, existing facilities in Texas, Florida or California. Such tests would clarify the biochemical changes taking place deep within the body as a result of spaceflight. The use of NMR is approaching the status of a routine procedure for the general public, with cost and availability as

the only limitations. NMR imaging is a completely noninvasive procedure causing no known harmful effects, and a superior technique for imaging live, soft tissue.

Publications: (1) Mondon, C.E., C.B. Dolkas, and G.M. Reaven. 1983. "Effect of confinement in small spaceflight size cages on insulin sensitivity of exercise-trained rats." AVIATION, SPACE AND ENVIRONMENTAL MEDICINE 54(10): 919-922. (2) Sandler, H., P. Webb, J. Annis, N. Pace, B.W. Grunbaum, D. Dolkas, and B. Newsom. 1983. "Evaluation of a reverse gradient garment for prevention of bedrest deconditioning." AVIATION, SPACE AND ENVIRONMENTAL MEDICINE 54(3): 191-201.

CNS CONTROL OF BODY TEMPERATURE AND METABOLISM 199-20-92-04

B.A. Williams, S.B. Kandasamy and T.S. Kilduff, Ames Research Center, Biosystems Division

As an important aspect in the control of the body's autonomic nervous system, temperature can be a reliable indicator of adaptation to stress in changing environments, such as the change in the effect of gravity during spaceflight. (The temperature biorhythm is often monitored as an indicator of stress.) Specific hypothalamic nuclei (in the vicinity of the pituitary gland) were identified as increasing glucose metabolism during fever through the anti-diuretic hormone (ADH), arginine vasopressin. This neuropeptide was known to control water retention to maintain appropriate blood pressure in the body. ADH also proved necessary to produce fever in rats that were deficient in that hormone. In addition, the endogenous opiate, endorphins, and enkephalin induced μ -type opiate receptors to greatly increase body temperature in rabbits and guinea pigs.

Other studies showed that the paratrigeminal nucleus in the medulla was the only brain structure to significantly increase the accumulation of the radioactive stain, (C^{14}) 2-deoxyglucose, in the brain of the ground squirrel (*Citellus lateralis*) during lowered temperatures resulting in hibernation. The paratrigeminal nucleus may be the brain's relay of thermal sensors from the face. (This task was successfully completed and terminated.)

Publications: (1) Kandasamy, S.B. and B.A. Williams. 1983. "Central effects of some peptide and non-peptide opioids and naloxone on thermoregulation in the rabbit." Environment, Drugs and Thermoregulation. Lomax, P. and E. Schonbaum, eds. New York: S. Karger. pp. 98-100. (2) Kandasamy, S.B. and B.A. Williams. 1983. "Hyperthermic responses to central injections of some peptide and non-peptide opioids in the guinea pig." NEUROPHARMACOLOGY 22: 621-628. (3) Kandasamy, S.B., and B.A. Williams. 1983. "Opposing action of dibutyryl cyclic AMP and GMP on temperature in conscious guinea pigs." NEUROPHARMACOLOGY 22: 65-70. (4) Kilduff, T.S., F.R. Sharp, and H.C. Heller. 1983. "Relative 2-deoxyglucose uptake of the paratrigeminal nucleus increases during hibernation." BRAIN RESEARCH 262: 117-123.

SIMULATED WEIGHTLESSNESS AND IMMUNE RESPONSIVENESS 199-20-92-07

A.D. Mandel, Ames Research Center, Biomedical Research Division

Hypokinetic/hypodynamic and anti-orthostatic responses to weightlessness and bedrest were simulated in mice using a suspension technique. Mice were chosen because their immune response is more sensitive than that of the rat's. Animals were suspended for one or two weeks in an anti-orthostatic (head-down) posture and were positioned to permit freedom of movement and eliminate load bearing by the hind limbs. Suspension resulted in reduced food and water intakes and a rapid 10% decrease in body weight to a level which was maintained for the remainder of the suspension period. Diuresis was evident in response to anti-orthostatic positioning, but the natriuresis and kaliuresis previously observed in the suspended rat were not evident. Hind limbs showed the greatest muscle atrophy in the soleus, followed by the gastrocnemius, the plantaris, and the extensor digitorum longus. Increased excretion of urea and ammonia were also noted in suspended mice. Post-suspension recovery was highly effective. These results demonstrated similarities in the responses of mice and rats to suspension. These studies expand the utility of the suspension model and suggest that the mouse may be useful in future physiological studies simulating both weightlessness and bedrest.

After one or two weeks of head-down suspension, mice showed a depressed α/β interferon production (Fig. 26). When the mice recovered for one week after release from suspension, they demonstrated a normal production capacity of interferon, and they exhibited a rebound effect of increased production of interferon. Keeping mice in the cold did not effect interferon production. These results indicated that stress was not responsible for the lowered immune responsiveness. To a certain extent the study supported the argument that changes in the immune system in space was caused by change in gravity, and not by stress.

Publications: (1) Caren, L.D., J.A. Leveque, and A.D. Mandel. 1983. "Effect of Ethanol on the Immune System in Mice." TOXICOLOGY LETTERS 19: 147-153. (2) Degre, M., K. Belsnes, H. Rollag, S. Beck, and G. Sonnenfeld. 1983. "Influence of the genotype of mice on the effect of interferon on phagocytic activity of macrophages." PROCEEDINGS OF THE SOCIETY OF EXPERIMENTAL BIOLOGY AND MEDICINE 173(1): 27-31. (3) Smith, P.K., D.E. Nerland, and G. Sonnenfeld. 1983. "Effect of interferon on murine cytochrome p-450: Effect of partially purified antigen-specific interferon gamma." JOURNAL OF INTERFERON RESEARCH 3(2): 219-222.

MONOCLONAL ANTIBODY PRODUCTION TO HUMAN T-CELLS 199-20-92-08

R.A. Goldsby, Amherst College, Amherst, MA, Department of Biology
A.D. Mandel, Ames Technical Monitor

Monoclonal antibodies were produced against a variety of antigens on the surface of T-lymphocytes. The procedure, called epitope ratio analysis

SUPPRESSION OF INTERFERON PRODUCTION DURING SIMULATED WEIGHTLESSNESS

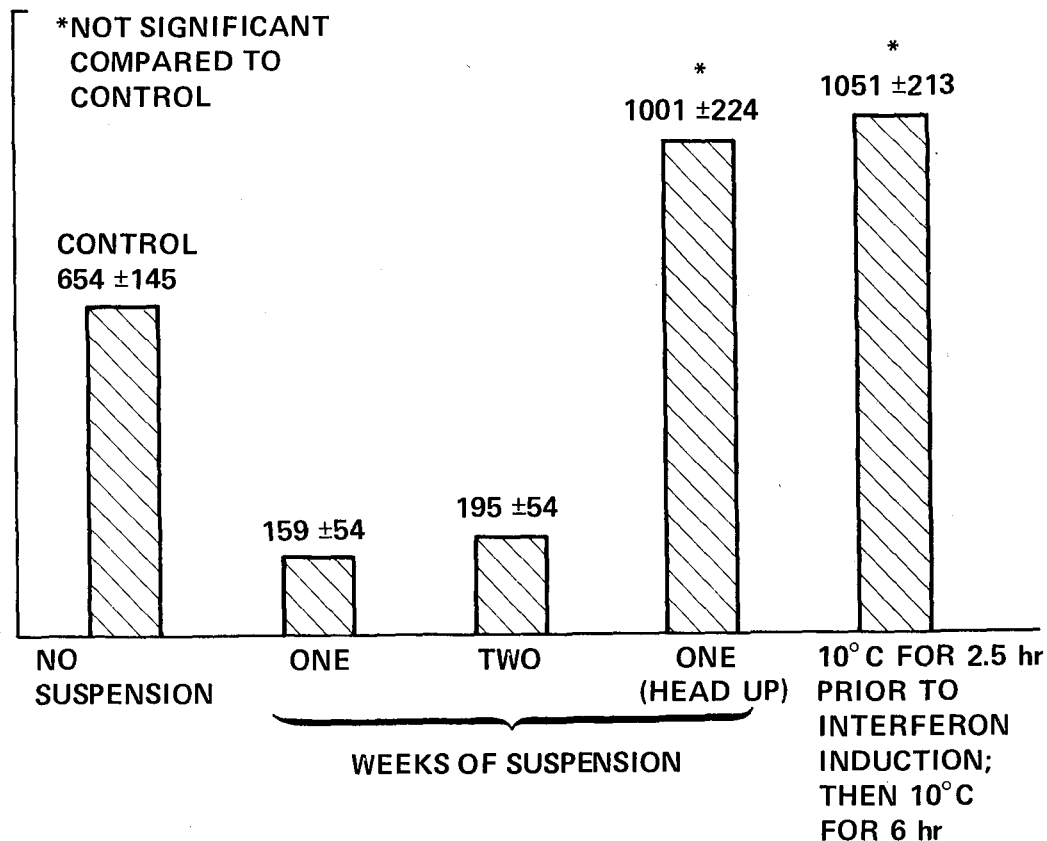


Fig. 26. Interferon production in mice measured in titers, expressed as the highest dilution of serum causing a 50% plaque (viral growth) reduction on murine L-929 cells by the Indiana strain of bovine vesicular stomatitis virus. (Mandel 199-20-92-07)

(ERA), measured the relative expression on human cell surfaces of specific cell antigens in vitro. This new procedure is applicable to many systems requiring measurement of such differential expression of antigens, and may be useful in the detection of infectious disease in astronauts prior to launch. (This task was successfully completed and terminated.)

Publications: none.

R.J. Wurtman, Massachusetts Institute of Technology, Department of Nutrition
and Food Science

C.M. Winget, Ames Technical Monitor

This research task concentrated on examining the effects of dietary choline, tryptophan, and tyrosine on the synthesis and action of the neurotransmitters: acetylcholine, serotonin and the catecholamines. Studies demonstrated that: (1) tyrosine levels determine the amounts of dopamine synthesized in, and released from, slices of rat brain caudate nucleus in vitro when these tissues are stimulated electrically (this system should allow us to dissect the mechanism that couples firing frequency to precursor-responsiveness); (2) animals kept for three to four days on a carbohydrate-free diet become "carbohydrate cravers" when again given the opportunity to choose carbohydrates, and this effect is independent of the sweetness of the test carbohydrates; (3) a serotonin-releasing drug, fenfluramine, can be used to diminish carbohydrate selectively in people; (4) food consumption elevates plasma and brain lysine levels in proportion to the food's protein content; and (5) dopamine increases phospholipid methylation in vitro. An experimental animal preparation was developed that allowed the study of tyrosine for helping people to cope with stress. An acute, mild electroshock in the rat depleted the brain of norepinephrine and caused subsequent changes in the animal's behavior.

Publications: (1) Gibson, C.J., C.J. Watkins, and R.J. Wurtman. 1983. "Tyrosine administration enhances dopamine synthesis and release in light-activated rat retina." JOURNAL OF NEURAL TRANSMISSIONS 56: 153-160. (2) Glaeser, B.S., T.J. Maher, and R.J. Wurtman. 1983. "Changes in brain levels of acidic, basic, and neutral amino acids after consumption of single meals containing various proportions of protein." JOURNAL OF NEUROCHEMISTRY 41: 1016-1021. (3) Leprohon, C.E., J.K. Blusztajn, and R.J. Wurtman. 1983. "Dopamine stimulation of phosphatidylcholine (lecithin) biosynthesis in rat brain neurons." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA 80: 2063-2066. (4) Reinstein, D.K., T. DeBoisser, N. Robinson, and R.J. Wurtman. 1983. "Radial maze performance in three strains of mice: Role of the fimbria/fornix." BRAIN RESEARCH 263: 172-176. (5) Wurtman, J.J., P.L. Moses, and R.J. Wurtman. "Prior carbohydrate consumption affects the amount of carbohydrate that rats choose to eat." JOURNAL OF NUTRITION 113: 70-78.

THE GRAVITATIONAL BIOLOGY PROGRAM IN NASA

The objective of gravitational biology is twofold: to provide an adequate base of fundamental biological information for future space missions, and to use the unique properties of the space environment to enlarge our concepts of terrestrial biology. It is the necessary prelude and foundation for the biological use and habitability of space. The answers we seek to questions vital to space habitation include: can plants and animals survive more than one generation in space; what minimum G load is required for normal development; and can some other stimuli like light or vibration be used as a substitute for gravity in space. The pervasiveness and antiquity of gravity's effect has shaped terrestrial life since its very origin. This makes gravity a unique and ideal tool that only NASA has the capability to fully manipulate and utilize. Ground-based research has not only led to flight experiments selected for Spacelab missions and also flown in the Shuttle orbiter and on Cosmos satellites, but has produced valuable results on the ground. For example, studies of the physiology of the inner ear have contributed significantly to understanding Meniere's disease, an affliction characterized by vertigo, nausea and progressive deafness that affects many people on Earth. Other gravitational studies are directed toward understanding the pathology of osteoporosis, an insidious crippler that accompanies aging especially in women; the physiology of lignification, the very structural fiber of plants; and the role of gravity in calcium mediated physiological mechanisms and calcium metabolism in both plants and animals. Gravitational biology research, therefore, forms a fundamental scientific foundation applicable to solving biological problems both in space and on Earth.

(From NASA Space Science and Applications Notice, October 25, 1982)

Thora Halstead
Program Manager

GRAVITATIONAL BIOLOGY

Development, leading to a mature organism, and the subsequent aging of the organism, is studied in the fruit fly (*Drosophila melanogaster*) (Fig. 27). This insect can be easily maintained at low cost, reproduces rapidly and has a well-defined genetic system. These characteristics make the *Drosophila* an attractive specimen for studies of developmental biology, aging and comparative anatomy. Oxygen consumption and cellular function are practically identical in *Drosophila*, mice, rats, and humans.

At several stages of development, *Drosophila* were flown on Cosmos biosatellites. Some of the flies mated and produced offspring in space, although multiple generations could not be studied because of the duration of the flights and the lack of separation between members of different generations. These joint US-USSR experiments in 1975 and 1977 also revealed that weightlessness had a life-shortening effect on adult flies taken into space (Fig. 28), but not on flies that were allowed to develop in weightlessness. An increased metabolic rate seemed to be linked to the decreased lifespan of adult flies. Despite these signs of accelerated aging during short-term flights, if animals or humans spent their entire lives in weightlessness, their lifespans may significantly increase because of an eventual reduction in metabolic rate.

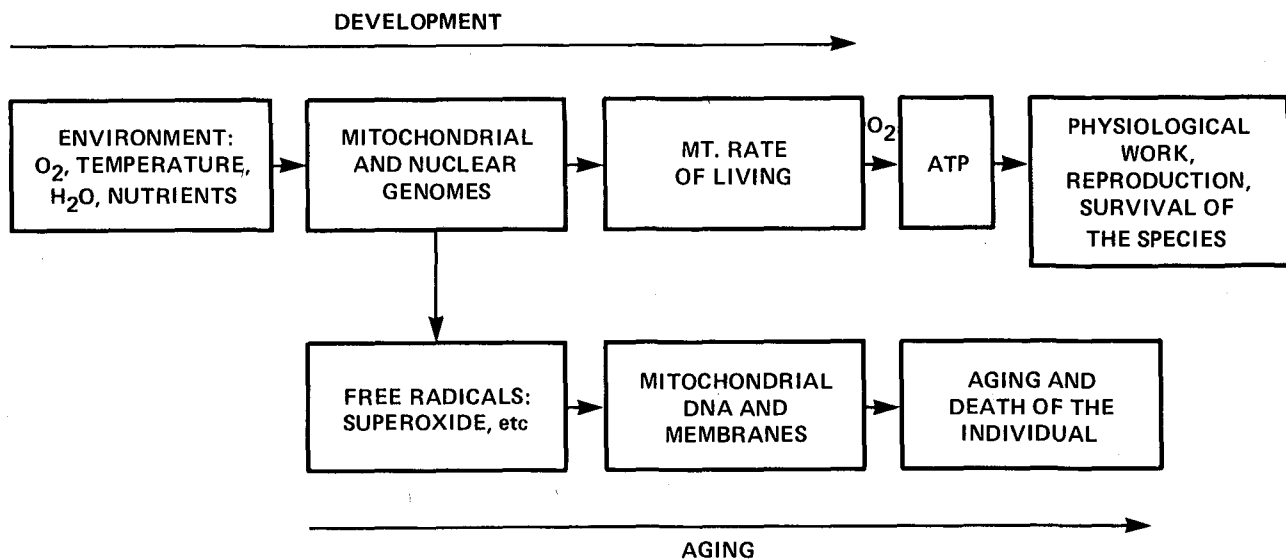


Fig. 27. Normal development appears to be sensitive to environmental factors, including oxygen tension, temperature, pH, the availability of water and nutrients, and radiation or other hazardous factors. In insects, and perhaps in higher organisms, aging is also sensitive to similar environmental factors. For example, in the diagram above the free radical theory of aging is shown whereby free radicals (superoxides and peroxides) are thought to damage mitochondrial DNA and cell membranes, resulting in aging and the ultimate death of the organism. (Miquel 199-40-22)

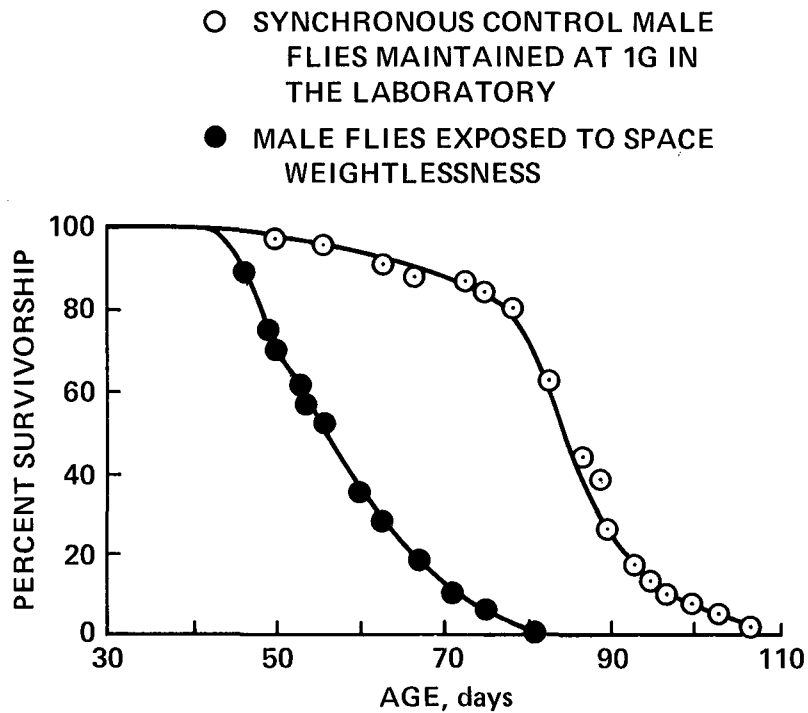


Fig. 28. Decreased lifespan in *Drosophila* during spaceflight. (Miquel)

During studies on Earth, examinations of structural changes on the cellular level showed mitochondrial alterations correlated with aging. Free radicals, or fragments of molecular oxygen as byproducts of respiration, caused gradual disorganization of mitochondrial DNA and membranes. This specific cause of aging resulted in decreased production of ATP by the mitochondria and reduced other cellular activity.

Striking similarities exist among studies and observations of aging in different organisms. During spaceflight the effects of weightlessness on *Drosophila* have been similar to the effects of abnormally high temperature; these environmental factors both induce an increase in the rate of oxygen use and a decrease in lifespan. In humans, deconditioning of the cardiovascular, respiratory and musculo-skeletal systems during spaceflight resemble conditions similar to those of normal aging. To further study the functional questions of aging and development in weightlessness, a small insect holder (Fig. 29) has been built to allow easy operation on any Space Shuttle mission. The device contains three, separate chambers, allowing for separation of males and females before flight, combining sexes inflight for mating and egg laying, and shaking the adult flies down to a bottom chamber after egg laying to separate them from the next generation. Depending on the length of the spaceflight, multiple generations could be hatched and segregated during a single flight. The simple operation of this device requires literally only seconds of crew time.

Further details on the implications of physiological aging and weightlessness can be found in NASA Conference Publication 2248, entitled "Space Gerontology."

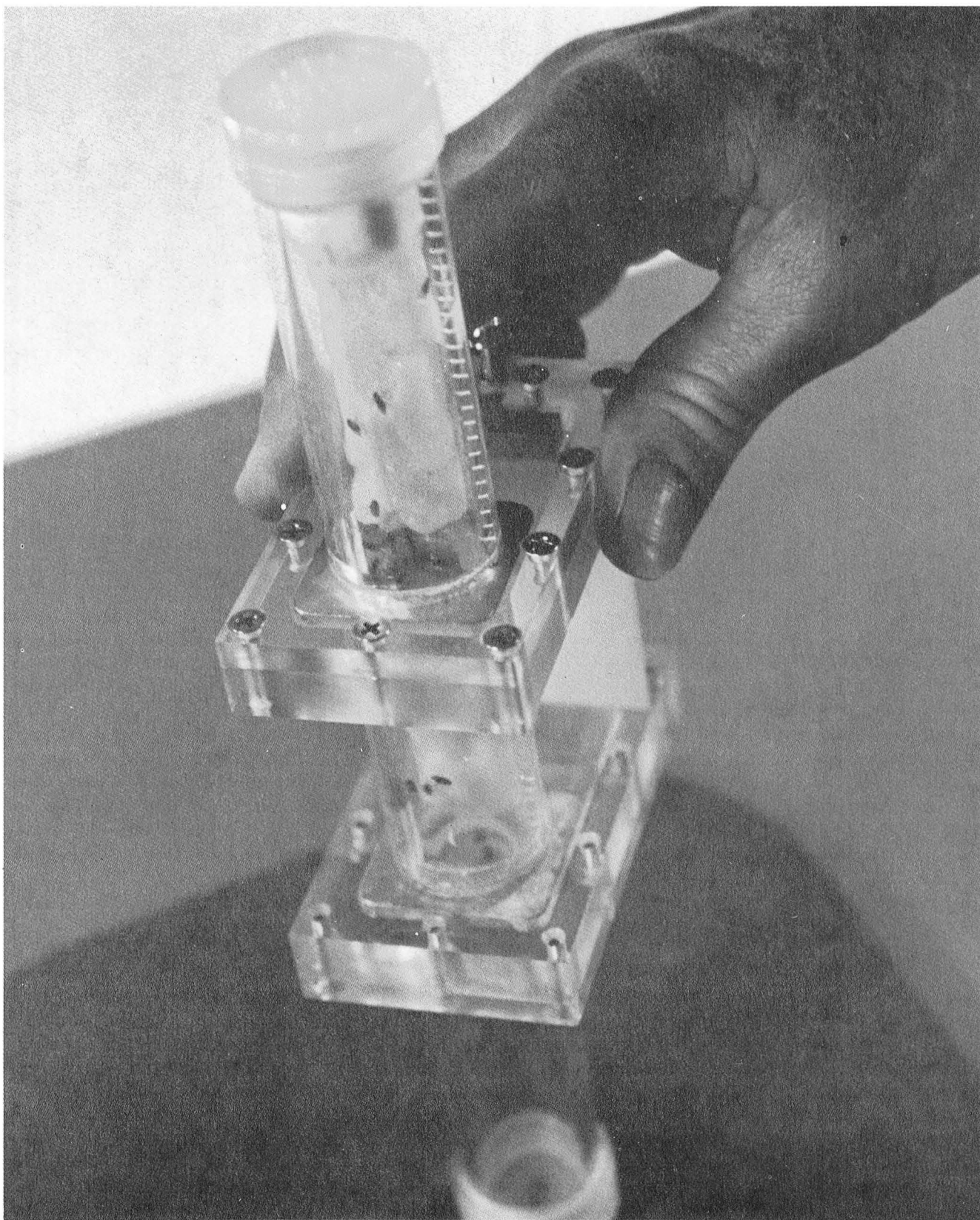


Fig. 29. Insect holding chamber for the study of development and aging in multiple generations during manned spaceflight. (Miquel 199-40-22)

EFFECTS OF WEIGHTLESSNESS AND HYPERGRAVITY ON DEVELOPMENT AND AGING OF DROSOPHILA 199-40-22-01

J. Miquel, Ames Research Center, Biomedical Research Division

The development time and adult lifespan of fruit flies (Drosophila melanogaster) significantly increased by about 20% when their nutrient medium was supplemented with nordihydroguaiaretic acid an inhibitor of mitochondrial electron transport, which resulted in a decrease of nearly 20% in the respiration rate of the imagoes (sexually mature adults). In addition, delayed eclosion (hatching) of adult flies rotated in centrifuges or clinostats was associated with altered respiration rates. A spinoff of this research on the effects of altered gravity on age-related mitochondrial changes led to the development of a new theory, which postulates that the initial senescent damage is a peroxidative degradation of the mitochondria by respiration-linked oxygen radicals.

Publications: (1) Anton-Erxleben, F., J. Miquel, and D.E. Philpott. 1983. "Fine structural changes in the mid gut of old Drosophila melanogaster." MECHANISMS OF AGING AND DEVELOPMENT 23: 265-276. (2) Miquel-Calatayud, J. 1983. "Aging science and fiction." MUNDO CIENTIFICO 1(7): 794-804. (3) Miquel, J. 1982. "Comparison between the weightlessness syndrome and aging." in Space Gerontology (NASA Conference publication 2248). Moffett Field, CA: Ames Research Center. pp. 1-7. (4) Miquel, J., and K. Lindseth. 1983. "Determination of biological age in antioxidant-treated Drosophila in mice." in Intervention in the Aging Process (Part B: Basic Research and Preclinical Screening). Regelson, W., and F.M. Sinex, ed. New York: Alan R. Liss. pp. 317-358. (5) Miquel, J., J.E. Johnson, and J. Cervos-Navarro. 1983. "Comparison of CNS aging in humans and experimental animals." BRAIN AGING: NEUROPATHOLOGY AND NEUROPHARMACOLOGY 21: 231-258.

BIOLOGICAL ADAPTATION

Understanding how organisms adapt to changes in gravity aids biologists in understanding the evolution of structures and functions among different species of plants, invertebrates and vertebrates. Biological processes studied under the aegis of the Biological Adaptation RTOP include structure, movement, and the transport and regulation of fluids and minerals. Manipulation of gravity below 1 G for more than a few seconds at a time can only be accomplished during spaceflight.

Investigators study varied organisms and their structural elements, such as cellulose and lignin in plants, and bone, cartilage and chitin in animals. In fact, calcium-modulating proteins (e.g., calmodulin) may have been a critical event in evolution of eukaryotes. The development of calcium as a regulator of cellular function and as a structural material may have allowed multicellular organisms to grow and multiply under Earth's gravity. If gravity played a role in the evolution of the calmodulin system, what would happen to this system after multiple generations living without stimulation of gravity in a weightless environment?

Bone specimens from laboratory rats flown for periods just under 20 days on three unmanned Soviet biosatellites (Cosmos 782, 936 and 1129) were analyzed by US investigators. The weight-bearing bones of the leg, the femur and tibia, reduced their rates of cortical bone growth. Both trabecular and cortical bone volumes decreased, although reduction of the trabeculae was more severe. Ash content of weight-bearing bones decreased, while marrow fat increased. Forelimb bones lost mineral, and the spinal column lost strength. The weight-bearing skeleton did not fully recover by 29 days postflight.

The naturally-occurring, ongoing processes of skeletal modeling also changed. Bone formation stopped almost completely, and bone resorption was virtually unchanged. Because bone formation was the larger of the two effects, spaceflight caused a net bone loss. Some impaired growth was noted in the jaws. Other skeletal elements, that undergo less active use by the organism and model at a slower rate, may show changes after periods of weightless flight longer than 20 days.

On Cosmos 936 a group of rats was subjected to artificial gravity (1 G) on a small centrifuge. This group's decrease in bone formation was similar to the weightless group, but bone mass recovered more rapidly postflight in the centrifuged group, and their femurs maintained normal strength. Centrifuges on Earth, as well as in space, are necessary for the scientific study of gravitational biology. Expertise from two decades of biological studies using the centrifuge facilities at Ames Research Center (ARC) allowed investigators of the Biomedical Research Division to contribute in design studies of a space centrifuge, or Variable Gravity Research Facility (VGRF). Since the early 1960s the Space Science Board of the National Academy of Sciences repeatedly encouraged the development of such a national research facility in space as a counterpart to the centrifuges on Earth at ARC. A VGRF on board Spacelab, or on a space station, would permit experiments

designed for less than 1 G but greater than zero G. Work began in cooperation with ARC's Biosystems Division for the determination of vibration tolerances and undesirable Coriolis effects for different species. (The longer the radius of the centrifuge, the greater the vibration.) Some engineering problems were similar to those in the development of the Vestibular Research Facility (see pg. 45), although the vestibular spinning and control mechanism was more complex, requiring variable speeds and two-axis gimbals. Solutions to these engineering questions may provide the space agency with an operational centrifuge that could be used as part of an astronauts' fitness regime in space to remedy the effects of spaceflight deconditioning.

On Earth, investigators simulate the physiological effects of weightlessness on organisms using systems that lift and partially unload weight from the hind limbs of rodents. Such a laboratory model produces results to compare with spaceflight data and allows researchers to investigate the underlying causes of changes in the major weight-bearing bones of the body. In this way a data base is created of results from flight and ground experiments to aid in the careful design of future research.

All biological flight studies thus far have been limited by a minimal number of specimens, and weightlessness exposures for brief periods of time, usually less than 20 days. Of particular interest in the future is the effect of long-term exposures of weightlessness on various animal and plant species over many months and spanning many generations. As an example, carrot cells have been able to divide and develop in weightlessness, but whether continuous generations could continue to grow is unknown. Except for missions of the Soviet Salyut space station, spaceflights are too short to see if plants can flower in weightlessness, or to see if animals can produce successive generations in weightlessness. Only biological experiments on long-term flights will permit scientists to finally understand the role of gravity on biological adaptation and function.

RECTAL TEMPERATURE RESPONSE OF RATS TO DIFFERENT G-LOADS AT 22.6 rpm MEANS \pm S.E. (6 RATS)

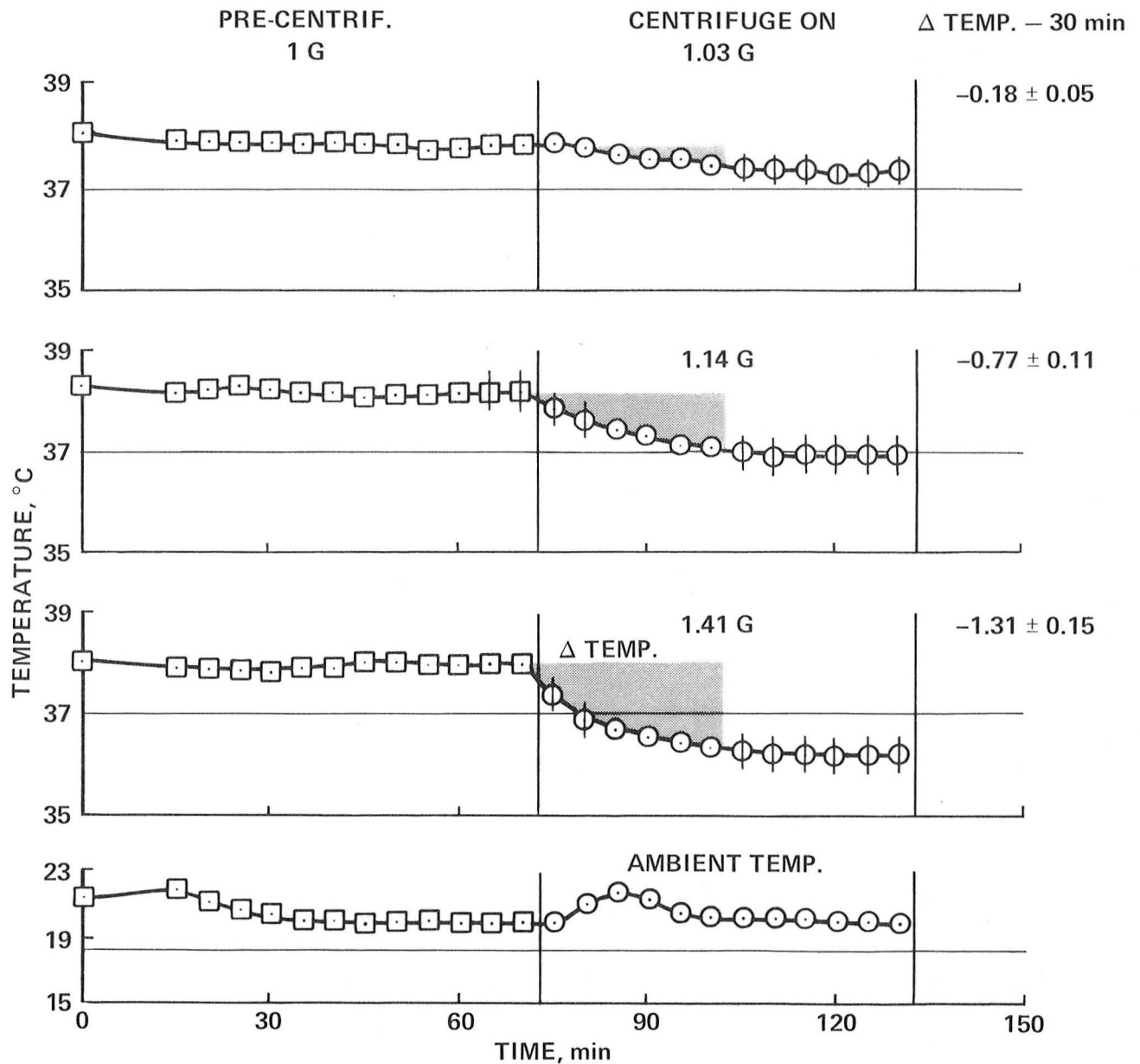


Fig. 30. Shaded area shows the decrease in rectal temperature during the first 30 min of centrifugation; the temperature decreases are also registered in numerals at the far right. As little as 0.11 G difference between the upper and middle curves will produce a significant difference in the rectal temperature response. Also, the top curve shows that as little as a 0.03 G difference from 1 G can produce a detectable change in temperature. Temperature is very sensitive to G-differences, which makes it very useful for future flight experiments employing rats as test subjects. (Oyama 199-40-32-01)

HYPER-GRAVITATIONAL EFFECTS ON METABOLISM AND THERMOREGULATION

199-40-32-01

J. Oyama, Ames Research Center, Biomedical Research Division

Studies continued on both short-term, stress effects and long-term adaptational effects of organisms in altered gravitational fields produced at the centrifuge facilities of the Biomedical Research Division. Investigators focused on quantifying changes in thermoregulation, gluconeogenesis (synthesis of glucose by liver and kidney from non-carbohydrate sources, i.e., amino and fatty acids), gluconeogenic hormones and their substrates, and glucose homeostasis.

In response to hypergravitational stress (greater than 1 G), the rectal and tail temperatures of rats (Fig. 30) were dependent on the gravitational intensity alone, and were unaffected by differences in the radius of the centrifuge or the rate of rotation. Tilted at plus or minus 29° rats exposed to hypergravity in either the head-up or head-down position showed the same temperature responses as rats in the normal horizontal position, demonstrating the refractory character of the thermoregulatory center to different body orientations. Finding the high sensitivity of the thermoregulatory system to gravitational force changes increases the usefulness and importance of the system as a physiological monitor of animals in spaceflight experiments.

Of the hormones affecting gluconeogenesis, insulin and glucagon sustained increases, and glycerol sustained a decrease during hypergravity. An initial, rapid rise in blood glucose to hyper-G stress was due mainly to an increase in gluconeogenesis. In addition, a procedure was developed for in situ liver perfusions of decapitated rats instead of intact, anesthetized rats. The new procedure allowed for the study of gluconeogenic rates in isolated hepatocytes that were free from any anesthetic drug action in the liver. Using the new procedure, comparative gluconeogenic rate measurements were initiated on isolated hepatocytes from hypergravity-stressed and control rats.

Publications: (1) Economos, A.C., J. Miquel, R.C. Ballard, M. Blunden, K.A. Lindseth, J. Fleming, D.E. Philpott, and J. Oyama. 1982. "Effects of simulated increased gravity on the rate of aging rats: Implications for the rate of living theory of aging." ARCHIVES OF GERONTOLOGY AND GERIATRICS 1: 349-363. (2) Oyama, J. 1983. "Metabolic effects of hypergravity on experimental animals." in Space Gerontology. Miquel, J. and A.C. Economos, eds. Moffett Field, CA: Ames Research Center, pp. 37-51.

**RENAL FUNCTION, WATER, ELECTROLYTE BALANCE, AND INTESTINAL TRANSPORT IN
HYPOKINETIC ANIMALS 199-40-32-02**

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Biophysics
E.M. Holton, Ames Technical Monitor

Suspending the hind limbs, and thus unloading the weight, of rats simulated many of the responses seen under conditions of weightlessness. These anti-orthostatic (head-down) rats responded with diuresis, natriuresis and kaliuresis (water, sodium and potassium excretion), which was also comparable to the response of volume loading of the thoracic blood vessels. After two weeks of suspension, loss of muscle mass resulted, which was reflected in decreased levels of muscle protein and RNA, but no change in DNA. The greatest loss occurred in the soleus muscle (used to support the body) followed by the gastrocnemius muscle (used for walking and jumping). The plantaris muscle (used to flex the foot) was less affected, and the extensor digitorum longus (used to extend the toes) was least affected. Older rats (525 g) lost 20% of their body weight during the first week of suspension, whereas growing rats (180-200 g) failed to gain weight. Decreases in muscle mass were comparable in older and growing rats. Initial observations suggested that much of the body weight lost was a decrease in fat content. Suspension also caused muscle fatigue at a faster rate with a lower force in the gastrocnemius than in any other muscle but caused no such fatigue in the soleus. These changes in the gastrocnemius appeared related to decreased electron transport by cytochrome C and decreased citrate synthetase activity.

Publications: (1) Musacchia, X.J. and J.M. Steffen. 1983. "The validity of an animal model for experiments related to weightlessness." *PHYSIOLOGIST* 26(6): S37-S40. (2) Musacchia, X.J., J.M. Steffen, and D.R. Deavers. 1983. "Rat hindlimb muscle responses to suspension hypokinesia/hypodynamia." *AVIATION, SPACE AND ENVIRONMENTAL MEDICINE* 54(11): 1015-1020.

STRUCTURAL DEVELOPMENT AND GRAVITY 199-40-32-04

E.M. Holton, Ames Research Center, Biomedical Research Division

To better model the effects of weightlessness in the rat on Earth, the rodent suspension system developed at Ames Research Center was upgraded. Elevating the hind limbs to remove the weight from antigravity muscles, the suspension line was attached above the rat to a movable crossbar on trolley wheels, which rolled across the top edges of the walls of the Plexiglas cage. Thus, the rat could move freely using its forepaws. The cage walls were easily raised to expand the cage as the rat grew.

The physiological effects of unweighting the hind limbs were compared with cold stress (40 C) after one or three weeks of exposure to each regime (Fig. 31). Adrenal weights, thymus weights, and corticosteroid levels were used as indicators of environmental stress. Changes in bone formation and apposition rates were measured using tetracycline labels. Bone formation

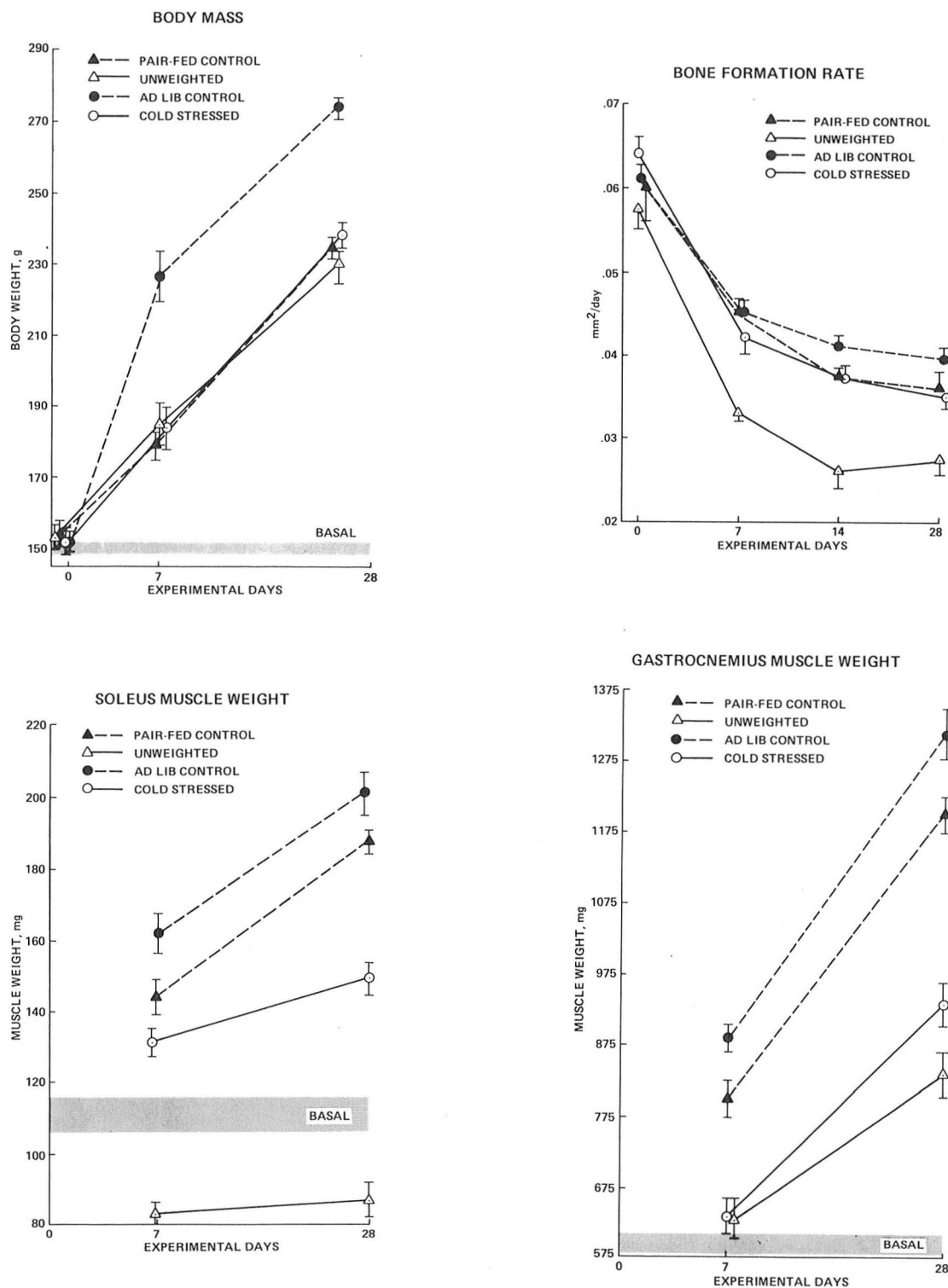


Fig. 31. Comparison of the physiological effects in rats from stress produced by lowered temperature or by unweighting the hind limbs, a simulation to produce effects similar to weightlessness. In pair-fed controls the amount of food was limited to the average amount consumed by the ad lib controls. (Holton 199-40-32-04)

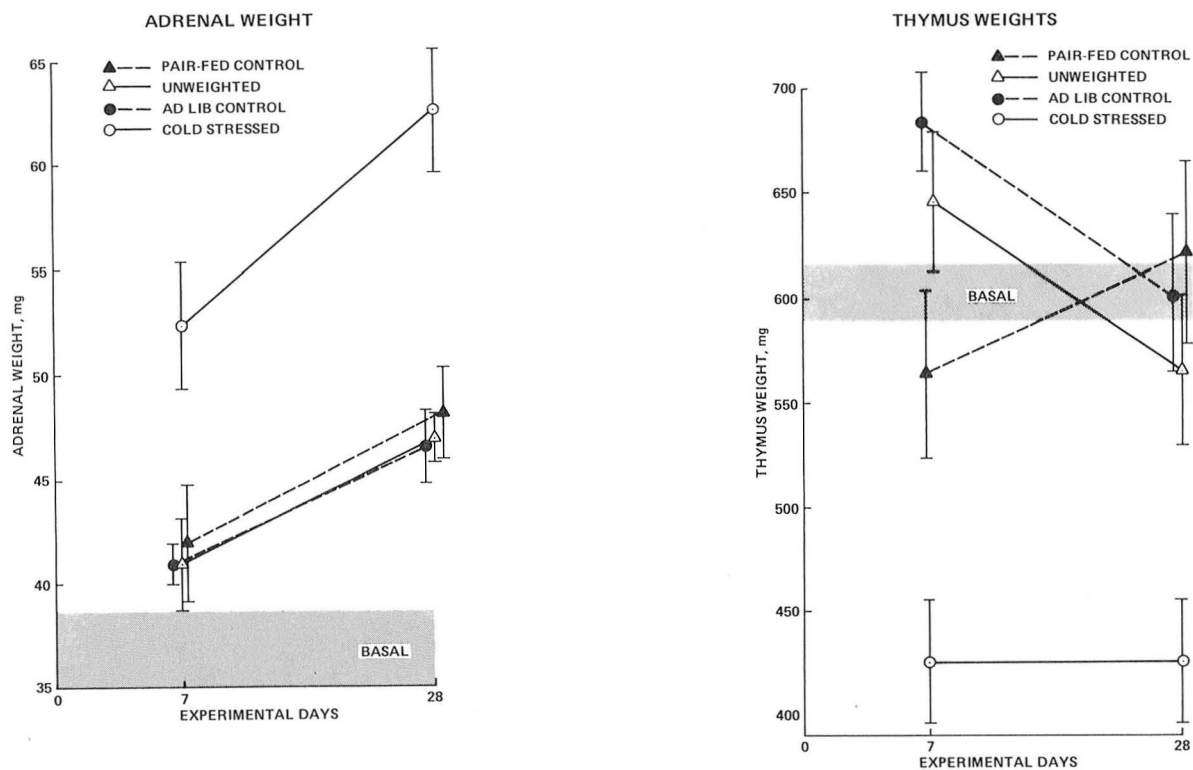


Fig. 31. (Holton 199-40-32-04)

rate in both unweighted and cold-stressed groups was 28% less than that of controls during the first week. By the third week, bone formation rate in cold-stressed animals showed a formation rate 20% less than controls.

A 17-month study using rats without suspension showed that cortical bone formation was most rapid at six weeks of age, and decreased sharply until approximately 18 weeks of age when it plateaued. Body mass, growth rate, and tibial microstructure were also compared from the juvenile to the adult rat.

Publications: (1) Bickle, D.D., R.K. Globus, and E.R. Morey. 1982. "Calcium transport from the intestine and into the bone in a rat model simulating weightlessness." *PHYSIOLOGIST* 25: 5143-5144. (2) Cann, C.E. and R.R. Adachi. 1983. "Bone resorption and mineral excretion in rats during spaceflight." *AMERICAN JOURNAL OF PHYSIOLOGY* 244(13): R327-R331. (3) Doty, S.B. and E.R. Morey-Holton. 1982. "Changes in osteoblastic activity due to simulated weightless conditions." *PHYSIOLOGIST* 25(6):

Sl41-Sl42. (4) Holton, E. 1983. "Bone and calcium alterations during spaceflight." in The Regulatory Functions of Calcium and the Potential Role of Calcium in Mediating Gravitational Responses in Cells and Tissues (NASA Conference Publication 2286). Roux, S.J., ed., Washington, D.C.: NASA. pp. 111-126. (5) Holton, Emily M. 1982. "Effects of weightlessness on bone and muscles of rats." in Space Gerontology (NASA Conference Publication 2248). J. Miquel and C. Economos, eds. pp. 59-66. (6) Jee, W.S.S., T.J. Wronski, E.R. Morey, and D.B. Kimmel. 1983. "Effects of spaceflight on trabecular bone in rats." AMERICAN JOURNAL OF PHYSIOLOGY 244(13): R310-R314. (7) Morey-Holton, E.R., M.D. Bomalaski, E. Enayati-Gordon, M.R. Gonsalves, and T.J. Wronski. 1982. "Is suppression of bone formation during simulated weightlessness related to glucocorticoid levels"? PHYSIOLOGIST 25(6): Sl45-Sl46. (8) Pace, N., E.R. Morey-Holton, D.F. Rahlmann, and A.H. Smith. 1982. Body Composition of 80-day Old and 270-day Old Rats after 14 Days of Hind-Quarter Suspension (EPL-82-2). University of California, Berkeley: Environmental Physiology Lab. pp. 1-79. (9) Wronski, T.J. and E.R. Morey. 1983. "Effect of spaceflight on periosteal bone formation in rats." AMERICAN JOURNAL OF PHYSIOLOGY 244(13): R305-R309.

EFFECT OF DECREASED GRAVITY ON CIRCULATION IN THE RAT 199-40-32-10

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E.M. Holton, Ames Technical Monitor

Limiting movement, or hypokinesia, in the anti-orthostatic (head-down) position mimicked the circulatory effects of weightlessness. Circulatory processes in the rats were studied during their exposure to head-down (-20°) hypokinesia, and during readaptation of the rats to control conditions. The cardiovascular measurements were done in control experiments on unrestrained, unanesthetized rats, and in the same animals in hypokinetic conditions, and during readaptation to free activity. Because surgery and anesthesia drastically decrease cardiac output and other circulatory parameters in rats, measurements were taken from unanesthetized rats. For sampling blood during the study, the aortas and right ventricles of the animals were permanently cannulated ten to 15 days before the experiment.

Investigators measured the hormones ACTH, corticosterone and prolactin by radioimmunoassay to monitor the stress imposed on the rats by placement of the suspension harness and by the head-down position. These stress hormones rose in the early exposure to anti-orthostatic hypokinesia, but after six to seven days of exposure the animals adapted to the unusual position, as judged on the return of these three hormones to their normal levels. Plasma catecholamines were also elevated on day one and day three of the antiorthostatic exposure. The plasma growth hormone level was decreased on day one. On day seven of the exposure, the plasma levels of both hormones were only slightly above the control levels. After release from the harness and after return to their own cages the hormone levels were again elevated, although not as much as during the antiorthostatic exposure. The elevation lasted two to three days. In harnessed animals that were orthostatic (not positioned head-down), the increase in the plasma level of stress hormones was very small and it lasted only a few hours on the first day. The level

of hormones was at or near control values during the next six days. Removal of harnesses did not induce any increase of studied hormones.

Investigators studied hormonal stress levels during 30-minute immobilization in rats, repeated 17 times during a period of 17 days. Adaption processes were completely absent during repeated immobilization, while during exposure to anti-orthostatic hypokinesia, the animals adapted after three to four days, and in the case of orthostatic hypokinesia this process was only a few hours long.

In other studies the ADH levels decreased the first day of exposure to antiorthostatic hypokinesia, but angiotensin II levels were only slightly elevated. Also, cardiac output in antiorthostatic rats followed circadian patterns four to seven days after initiation of hypokinesia.

Publications: none

LIFE SCIENCES FLIGHT EXPERIMENTS

LIFE SCIENCES FLIGHT EXPERIMENTS PROGRAM IN NASA

The goal of the Life Sciences Flight Experiments Program is to establish a multi-use, multi-mission biomedical laboratory using Spacelab (SL). This will provide an opportunity for investigations of the effect of the space environment on biological systems that cannot be performed on the ground, with an emphasis on characterizing and understanding the problems of humans in spaceflight. A major feature of the program is the development of an inventory of Spacelab equipment which may be flown on many missions and serve the needs of multiple investigations on each mission. The near-term objective is to fly dedicated Spacelab missions at two-year intervals. Dedicated missions allow a maximum number of integrated experiments to be flown at one time, thus permitting extensive, simultaneous measurements on the limited set of specimens available on each flight. Such broad coverage provides numerous opportunities to correlate measurements from diverse experiments to characterize the biological effects of microgravity. Approximately 15 to 20 investigations will be carried out on each mission, with the first laboratory dedicated to the life sciences, Spacelab 4, scheduled for a January 1986 launch. Major efforts are also underway to fly a double rack of experiments on SL-1 and three racks of equipment on SL-3. Smaller scale experiments have been flown on STS-2 and STS-3 and will be flown on SL-2.

(From NASA Space Science and Applications Notice, October 25, 1982)

Tom Perry
Program Manager

The near weightlessness of spaceflight remains the definitive environment to test hypotheses developed during ground-based research in gravitational biology and space medicine (Fig. 32). Over the past two decades the Life Sciences Directorate at Ames Research Center has developed a multitude of experiments for spaceflight programs, such as Biosatellite (unmanned Earth orbital), Gemini, Apollo, Skylab, the Viking mission to Mars, joint US-USSR Cosmos biosatellites and the Space Shuttle. In the near future, life sciences experiments are scheduled primarily for flights of the Space Shuttle and Spacelab. These experiments only require seven to ten days of weightlessness that the Shuttle-Spacelab flights provide. Experiments requiring weightlessness for many weeks, months or years must wait for long-duration, unmanned satellites or a manned space station.

Spacelab, a pressurized module carried in the cargo bay of the Space Shuttle, provides a shirt-sleeve environment for scientists, both mission specialists and payload (non-career astronaut) specialists. Spacelab,

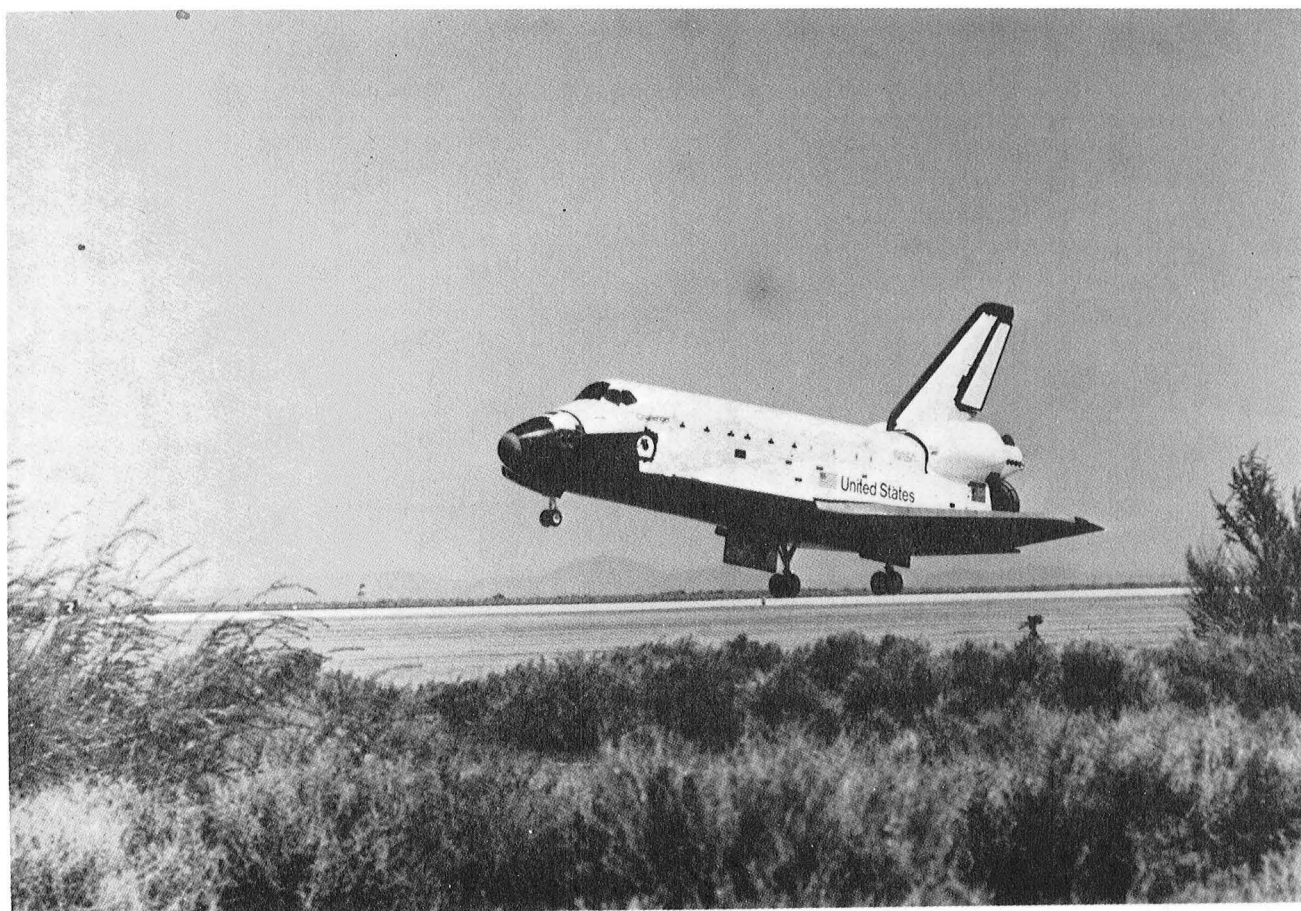


Fig. 32. The Space Shuttle provides scientists with a controlled environment to conduct biological and medical experiments in space.

built jointly by ten European nations through the European Space Agency (ESA), provides an environment where scientists can conduct biological experiments under standard laboratory conditions. Some of the necessary, specialized equipment for Spacelab is being designed and built by the Life Sciences Flight Experiments Project Office (LSFEP) at Ames Research Center.

Among the hardware projects for NASA's many plant and animal experiments, LSFEP is building a Research Animal Holding Facility to provide housing cages, environmental control, food, water, light, and waste management for various animal species. In the cages, wastes are blown down through a coarse grill in the floor onto a screen for drying. Urea and ammonia are trapped on a chemical and charcoal bed to control odors. Controlled lighting and air flow permit an environment for animals that is separate from humans. Another unique piece of equipment is the General Purpose Work Station (GPWS), an enclosed workbench to be used for animal surgery and any other laboratory techniques. Like a fume hood in laboratories on Earth, the GPWS provides air flow within a confined area. The GPWS can be accessed by a sliding door, or by a laboratory glove box to completely isolate the working space from the spaceflight cabin. Such equipment is designed on the principle to perform only those laboratory procedures in space that cannot be delayed until return to Earth.

Life science investigations on Spacelab are performed by scientists from Canada, Italy, Switzerland, U.K., U.S.A., and West Germany. Spacelab missions carrying biological experiments will be either multidisciplinary (Spacelab 1, 2 and 3 from 1983 through 1985), or will be completely dedicated to life sciences (Spacelab 4 in 1986). Typical questions addressed on flight experiments are: (1) What is the role of gravity in a variety of biological processes, such as reproduction, growth and development, and spatial orientation and perception; and (2) how does the human body react to spaceflight? The following flight activities describe the current involvement of the Biomedical Research Division (LR) in basic biomedical and gravitational biology experiments using various species on flights of the unmanned Cosmos biosatellite, the Space Shuttle and Spacelab.

STS-8 ACTIVITIES AND EXPERIMENTS

Continuous Flow Electrophoresis System (CFES)

R.E. Grindeland evaluated the efficiency of the separation in weightlessness of rat pituitary cells during the eighth flight of the Space Transportation System (STS-8). The separation of the six types of pituitary cells into many different fractions allowed a choice of cells for culturing to produce the greatest possible quantities of hormones. Thus, efficient separation can increase the production of pituitary hormones for clinical and research use. STS-8 can be considered as a test run for this procedure. Preliminary results indicated a good separation (48 fractions in space compared to 20 on Earth), but a small yield (20% in space compared to 90% on Earth). A larger yield of cells may be possible by changing some operational parameters of the CFES. In the microgravity environment on STS-8, mixtures of pituitary cells in two different buffers secreted significantly less growth hormone than cells maintained on Earth, suggesting that weightlessness caused some form of secretory lesion.

Intra-ocular Pressure Experiment

D.E. Philpott acted as a consultant for the intra-ocular pressure experiment to determine if pressure in the eye increases during orbital flight. Excessive intra-ocular pressure can collapse capillaries in the eyeball, reduce peripheral vision, and cause other symptoms of glaucoma. An aplanation tonometer, recommended by Dr. Philpott, was used inflight. Results on self-administered tests by one astronaut were inconclusive pending revised procedures and further testing.

The Effects of Weightlessness on Arthritis

D.J. Weber, Student Investigator, Cornell University, Ithaca, NY
E.M. Holton, Project Manager/Scientist, Ames Research Center,
Biomedical Research Division
D. Larson and M. Ernest, Scientific Sponsors, Pfizer, Inc.
T. Kessler and G. Huston, Engineering Sponsors, General Dynamics, Inc.

Flight verification of the hardware for this experiment was conducted on STS-8. The Animal Enclosure Module (AEM) adequately supported six healthy rats without compromising the health, safety or comfort of the crew (Fig. 33). The experiment was among those chosen in a nationwide competition, the Shuttle Student Involvement Program (SSIP) sponsored by NASA and the National Science Teachers' Association. The experiment was designed by Daniel J. Weber while attending Hunter College High School in New York City, and is currently scheduled for flight on STS-11 in 1984. He hypothesized that arthritis relief from submersion in water on the Earth may be duplicated during weightlessness with a possible relationship to skeletal unloading and calcium loss during spaceflight. Rats will be inoculated before flight with adjuvant arthritis and the progress of the disease compared to Earth-bound rats after flight.

ANIMAL ENCLOSURE MODULE

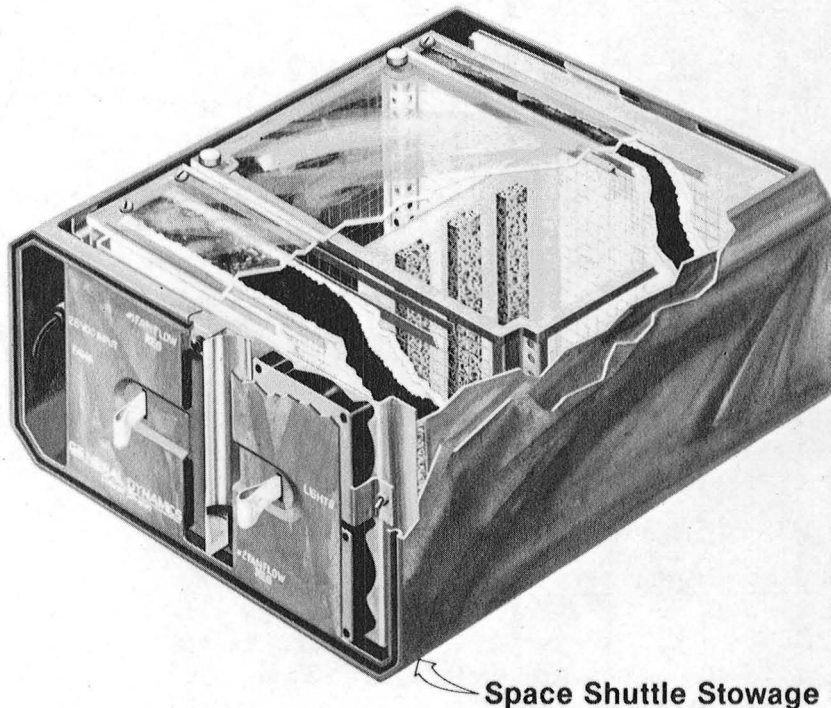


Fig. 33. The Animal Enclosure Module was test flown on STS-8 with six rats prior to a student Shuttle experiment on STS-11.

In preliminary experiments on Earth, rats were inoculated with adjuvant arthritis and their hind limbs were suspended unweighted for a duration similar to that of a Shuttle flight. They did not develop systemic inflammation or joint deterioration to the same degree as did control rats, although deterioration of the joint at the injection site was similar in all animals. Inoculated animals removed from the suspension device after one week did not develop the systemic disease during the following two weeks. The upcoming flight experiments will use three healthy rats and three inoculated rats both in orbit and on the ground. Although the number of animals per group will be small, the number should be sufficient to answer the hypothesis.

This SSIP experiment required the development of a flight-qualified container for rodent-sized animals because none existed. The AEM was designed and built by General Dynamics for less than \$100K, and may be donated to NASA for future flight experiments. Although promising experimental hypotheses can be easily tested in the AEM, no inflight handling of animals is possible with this system. Use of the AEM proved that carry-on experiments, stored in the mid-deck of the Space Shuttle cabin, provides an excellent opportunity to quickly and inexpensively process an experiment from conception to flight.

COSMOS 1514 EXPERIMENT

Cooperation between the USA and the USSR in the area of space biology and medicine began in 1971 with the signing of the US-USSR Science and Applications agreement. Annual meetings between the two countries created a joint program to fly biological satellites. The principal objectives of these flights were to determine how stresses of spaceflight affect biological systems with particular attention on biomedical problems common to humans and animals. Experiments in space biology and radiation physics were also conducted on these flights. Payloads contained rats, plants, insects, and a variety of other organisms.

This cooperative venture gleaned valuable data for all researchers involved, and was especially useful at a time when independent American biological flight experiments were not possible, due to the Space Shuttle being in the developmental stage. Considerable insight was also gained into Soviet experimental techniques and spaceflight operations. The flights included Cosmos 782 (1975), Cosmos 936 (1977), Cosmos 1129 (1979), and Cosmos 1514 (1983).

"Krovotok" - Cardiovascular Parameters during Spaceflight

V.P. Krotov, Principal Investigator, Institute of Biomedical Problems,
Moscow

B.S. Kulaev, Institute of Biomedical Problems, Moscow

H. Sandler, Ames Research Center, Biomedical Research Division

H.L. Stone, University of Oklahoma, Health Sciences Center

Cosmos 1514 was the first flight in this series to use an animal surrogate much more closely related to man than the rat. The rhesus monkey (Macacca mulatta) flew for five days to document hemodynamic changes of circulation to the head. Biotelemetry instruments documented the monkey's cardiovascular adaptation during the early stages of exposure to weightlessness and during the stress of reentry. This information had never been obtained in animals previously. Analysis of the data is being conducted.

The cardiovascular instrumentation represented a significant advance in transducer design. Measurements were taken from extremely small vessels (2-3 mm dia) without their invasion. Blood flow is detected using ultrasonic crystals, while blood pressure is detected by aplanation (20% constriction) of the vessel wall using an implantable strain-gauge cell with a 4.5 mm dia. Accurate readings of blood flow and pressure were obtained in the chronically-instrumented monkey on Earth prior to flight.

SPACELAB 2 EXPERIMENT

Vitamin D Metabolites and Bone Demineralization

H.K. Schnoes, Principal Investigator, University of Wisconsin
H.F. DeLuca, University of Wisconsin, Department of Biochemistry
E.M. Holton, Ames Research Center, Biomedical Research Division

Active metabolites of Vitamin D increase the transport of calcium from the intestine, as well as mobilize calcium from old bone. The alteration of this function during spaceflight will be monitored by measuring Vitamin D_2/D_3 (D_2 : ergosterol, from plants used to fortify milk/ D_3 : cholecalciferol, in animals) and its active metabolites: $25\text{-OH-}D_2/D_3$; $24,25(\text{OH})_2D_2/D_3$; and $1,25(\text{OH})_2D_3$. For this purpose blood samples will be taken from astronauts preflight, soon after entering orbit, just prior to reentry, and postflight.

SPACELAB 3 ACTIVITIES AND EXPERIMENTS

Research Animal Holding Facility (RAHF)

A research team led by P.X. Callahan and J.W. Tremor of the Biosystems Division, and including R.E. Grindeland, L.M. Kraft and P.R. Lundgren of the Biomedical Research Division (LR), will record animal growth, body composition, organ weights, and concentrations in blood plasma of electrolytes, hormones and cells. These results, with additional data from flight and ground-based studies on food and water consumption, biological rhythms, environmental conditions, and behavior, will enable an assessment of the performance of the RAHF. Comparison will also be made with rats flown by LR life scientists on three joint US-USSR biosatellite missions.

A Preventive Method for the Zero-gravity Sickness Syndrome: Autogenic Feedback Training for Vestibular Symptomatology

Biomedical results from Skylab indicated that, while individuals experienced different susceptibility to the nausea of space motion sickness, they adapted to weightlessness within five to seven days. Since current Shuttle missions are of this duration, it is desirable to ameliorate space motion sickness during the susceptible period. On Earth, human subjects successfully suppressed their own motion sickness symptoms using Autogenic Feedback Training (AFT). In this Spacelab experiment, crew members during preflight training will be instructed in specific exercises (operant conditioning) to volitionally control a variety of physiological parameters, e.g., heart rate, respiration rate, galvanic skin response. The subject's degree of control will then be tested during motion sickness tests, e.g., while moving the head during angular acceleration in a rotating chair. During flight a small instrument package on the body will monitor and display to the crew member the same physiological parameters used during training. AFT effectiveness in controlling any space motion sickness symptoms experienced by the crew members will be determined. (For further information on the progress of this experiment, see pg. 27.)

SPACELAB 4 EXPERIMENTS

Electron Microscopy, Electromyography, Protease Activity of Rat Hind Limb Muscles

D.A. Reilly, Principal Investigator, University of California Medical Center, Department of Anatomy
S. Ellis, Ames Research Center, Biomedical Research Division

Astronauts in space experienced a loss of muscle mass and strength, particularly in the calf of the leg. Muscles of rats also showed atrophy during Soviet space flights. Ground studies of muscle disuse in rats revealed a 30% loss of hind limb muscle mass in three to four days, and a 60% loss in 14 days. Spacelab will provide an essentially weightless environment to study atrophy, as opposed to such Earth-bound methods as immobilization, or denervation (severing the nerve to the muscle). This experiment proposes for the first time to assess changes due to weightlessness alone by removing the soleus and gastrocnemius muscles of some rats during spaceflight to prevent the body's repair processes when the animals are returned to Earth. While in orbit, tissue will be fixed for electron microscopy or frozen for histochemical and biochemical analysis on the ground. Other rats will be autopsied on the second and 22nd days postflight, the latter of which will also be implanted with electromyographic (EMG) transmitters prior to launch of the Shuttle. The number of muscle impulses monitored by EMG should decrease by 5% to 15% per day, reflecting the change in muscle workload. Among other measures of the atrophy process, studies will include determining the number of cellular lysosomes, which contain enzymes (proteases) to break down protein, and assessing the degeneration of energy-producing mitochondria. Results should establish or define any unique changes induced in skeletal muscle due to the weightless environment, and the rate that muscle atrophies in weightlessness as compared to atrophy produced on Earth by disuse, denervation, or cast immobilization.

Ground-based studies have led to the development of a more sensitive method for the measurement of Ca^{2+} -activated protease in rat muscles using much smaller samples than previously possible. Atrophying soleus muscle has sustained a 50% increase in the calcium-activated protease after four days of inactivity.

Bone, Calcium, and Space Flight

E.M. Holton, Principal Investigator, Biomedical Research Division
C.E. Cann, University of California Medical Center, Department of Radiology
W.E. Roberts, University of the Pacific Dental School

In growing rats flown for three weeks aboard the Soviet biosatellites, Cosmos 782, 936, and 1129, bone formation ceased in the diaphyseal (long portion of the limb bone) tibia, probably sometime after the eleventh day of flight. The proposed Spacelab experiment will use rats to expand our

current understanding of calcium turnover in the body and alteration of bone formation occurring during spaceflight. The rate of bone formation will be determined by using a fluorescent, bone-labelling technique. The histology of specific bones, such as the weight-bearing tibia, and the nonweight-bearing humerus and radius, should indicate growth rates of bone at these various, individual sites compared to the total skeleton. Isotope studies immediately after spaceflight will define those cells which are active. Total bone resorption by the body will be measured using a stable calcium isotope released from the bone. Changes in bone formation rate may be more difficult to remedy than changes in resorption, since most endocrines and drugs affect the latter. Also, if cell activity ceases, rather than merely decreases, recovery might be more difficult and possibly age-dependent. Once the specific defects and time span are known, then logical countermeasures can be formulated.

Frog Egg Fertilization and Development during Spaceflight

K.A. Souza, Principal Investigator, Biomedical Research Division
E. Nace and M. Ross, University of Michigan, Department of Biological Sciences

While mature organisms can survive in space, it is not yet known if the fertilization of eggs and the initial stages of embryogenesis will occur in weightlessness. This study will provide an important link for understanding

ESTABLISHMENT OF EMBRYONIC AXES IN XENOPUS

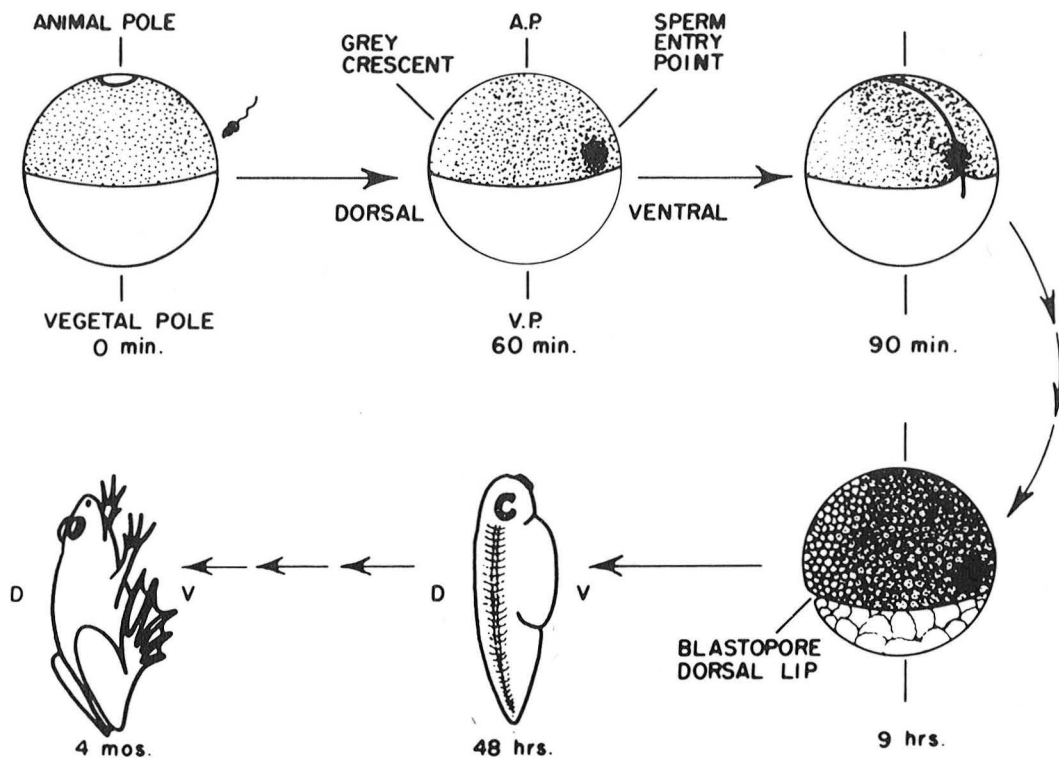


Fig. 34.

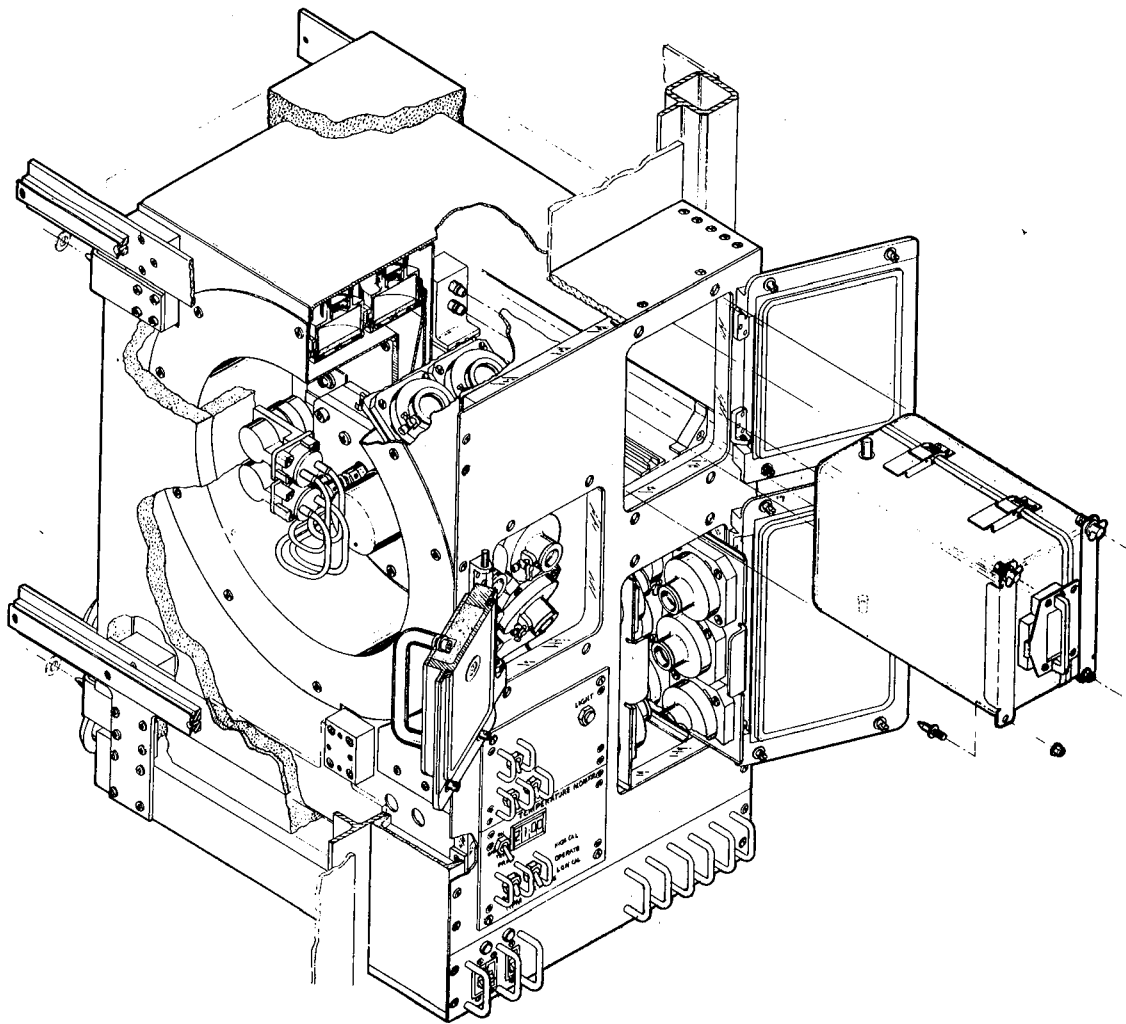


Fig. 35. The Spacelab amphibian environmental unit, containing small, circular storage chambers (bottom front) for frog eggs, a larger module for adult frogs (top front), and a small centrifuge (cut-away view) to provide a 1 G control for eggs.

the role that gravity plays in the fertilization and early development of the amphibian. Male and female gametes of the African clawed frog (*Xenopus laevis*) will be flown and examined for signs of successful fertilization, growth and organization of cells, through the blastula and gastrula stages into integrated organisms (Fig. 34). In amphibians, dorsal/ventral axis formation appears to be set at the time of sperm penetration. An important issue in developmental biology is whether this axis can develop without the influence of gravity. In addition to determining the role of gravity on fertilization, egg rotation, and the development of axis formation the development of the inner ear structure and associated components that are sensitive to gravity will be examined.

During FY 1983 design of the flight hardware was completed (Fig. 35) and passed the Critical Design Review. Fabrication then started on the Spacelab amphibian environmental unit. Prototype egg chambers and containers for adult frogs were built and tested successfully. A fixative was also tentatively selected for use inflight.

ADDITIONAL ACTIVITIES

ADDITIONAL ACTIVITIES

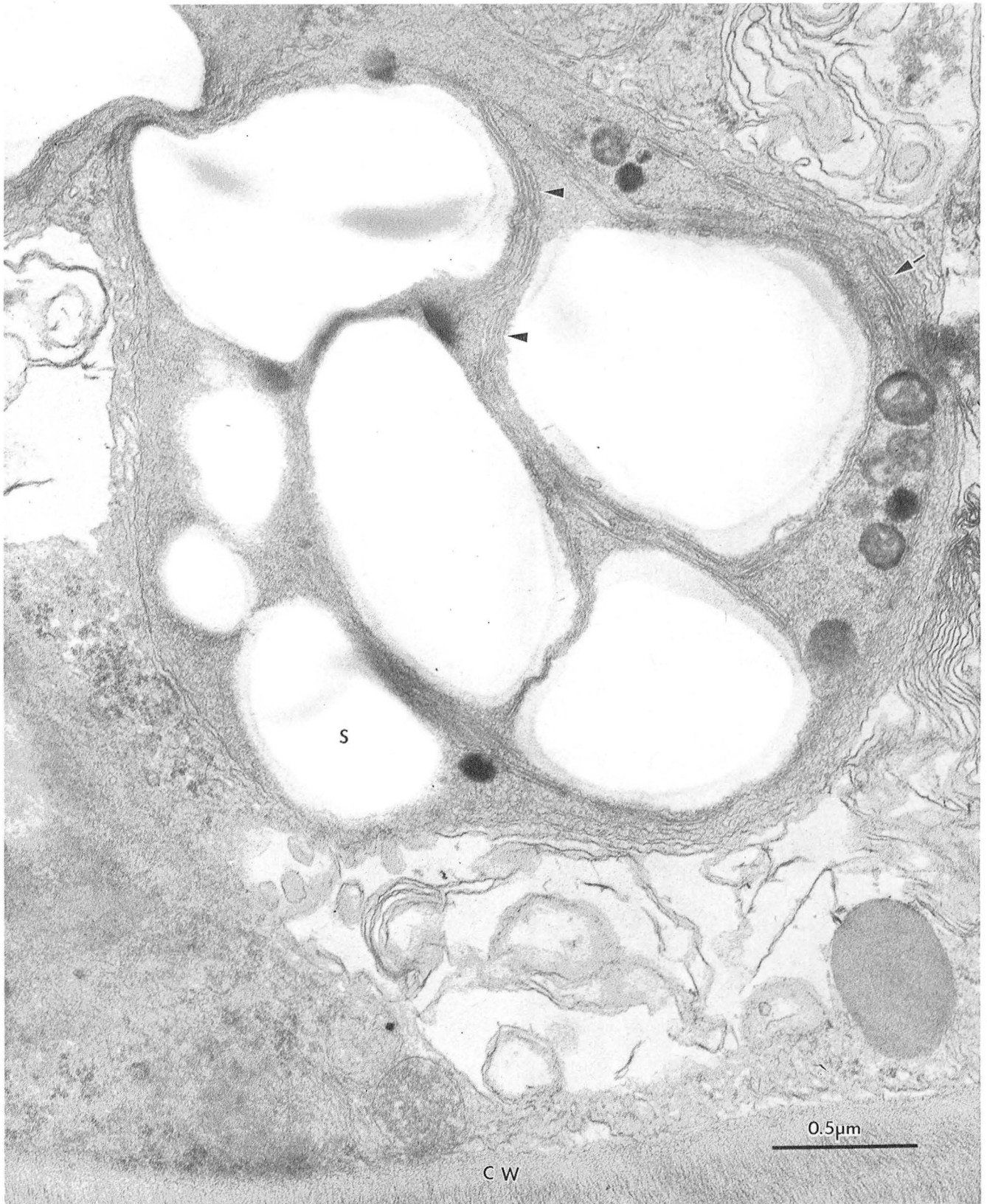


Fig. 36. Guard cell plastid from *Phragmipedium longifolium* (Orchidaceae) with well-developed thylakoids stacked in grana (arrow heads), and stroma lamellae (arrow). Abbreviations: S - starch, CW - cell wall.

Electron Microscopy and Plant Research

In addition to studies on the ultrastructure of animal cells, the Electron Microscope Facility provided support for plant research at Ames Research Center. R. A. Hill used the scanning electron microscope (SEM) to analyze hydroponically-grown lettuce roots by imaging their rhizoplane, the contact area between microbial populations and the root. SEM analysis was used to identify both rod-like and cocci bacteria on the roots' surfaces. R. A. Hill of Morgan State University conducted this study to assist research on the analysis of food crops produced in controlled ecological life support systems (CELSS).

For long-duration spaceflight involving many people, a bioregenerative life support system would recycle water, food and breathable gases, thus conserving supplies and reducing the mass of the life support system. Both hydroponic and aeroponic plant growth are studied as part of the CELSS program managed by the Advanced Life Support Office under the Extraterrestrial Research Division at Ames. This division investigates the origin, evolution and distribution of life and life-related chemicals throughout the universe, as well as researches the interrelationship of biological factors in small-scale and global habitats.

As the result of another study E. D'Amelio, in collaboration with Stanford University and the Biomedical Research Division, presented a paper entitled, "Structural and functional divergence of the guard cell plastids in Orchidaceae," at the annual meeting of the American Society of Plant Physiologists at Fort Collins, CO. The study focused on fourteen genera of orchids observed, first, under fluorescence microscopy. A red fluorescence was associated with photosystem II (PSII), the photosynthetic process that generates energy through the photolysis of water. Different values of red fluorescent intensity were found in the plastids from the different genera. The electron microscopy showed variations in the stages of development and stacking of the thylakoids in these plastids. These variations were correlated with the values of red fluorescence.

Guard cells of Paphiopedilum harrissianum and Paphiopedilum insigne have plastids devoid of true thylakoids and lacking red fluorescence. Haemaria discolor has a wide range of plastid stages with proplastids, amyloplastids (starch-containing), and elongated stages, developing perforated stroma lamellae. Some proplastids exhibit paracrystalline inclusions with a highly ordered substructure. Haemaria discolor has mostly negative red fluorescence, although some weak positive values were detected.

Phragmipedium longifolium (Fig. 36) and Vanilla aromaticum have well developed stroma thylakoids and grana. Both species have positive red fluorescence. The findings from the ultrastructural study and the values of fluorescence microscopy point towards a broad evolutionary divergence in the guard cell plastids of Orchidaceae.

E. D'Amelio was also invited to lecture at the first International Prochorophyta Symposium sponsored by NASA at the Scripps Institute of Oceanography. She spoke on collaborative research with San Jose State

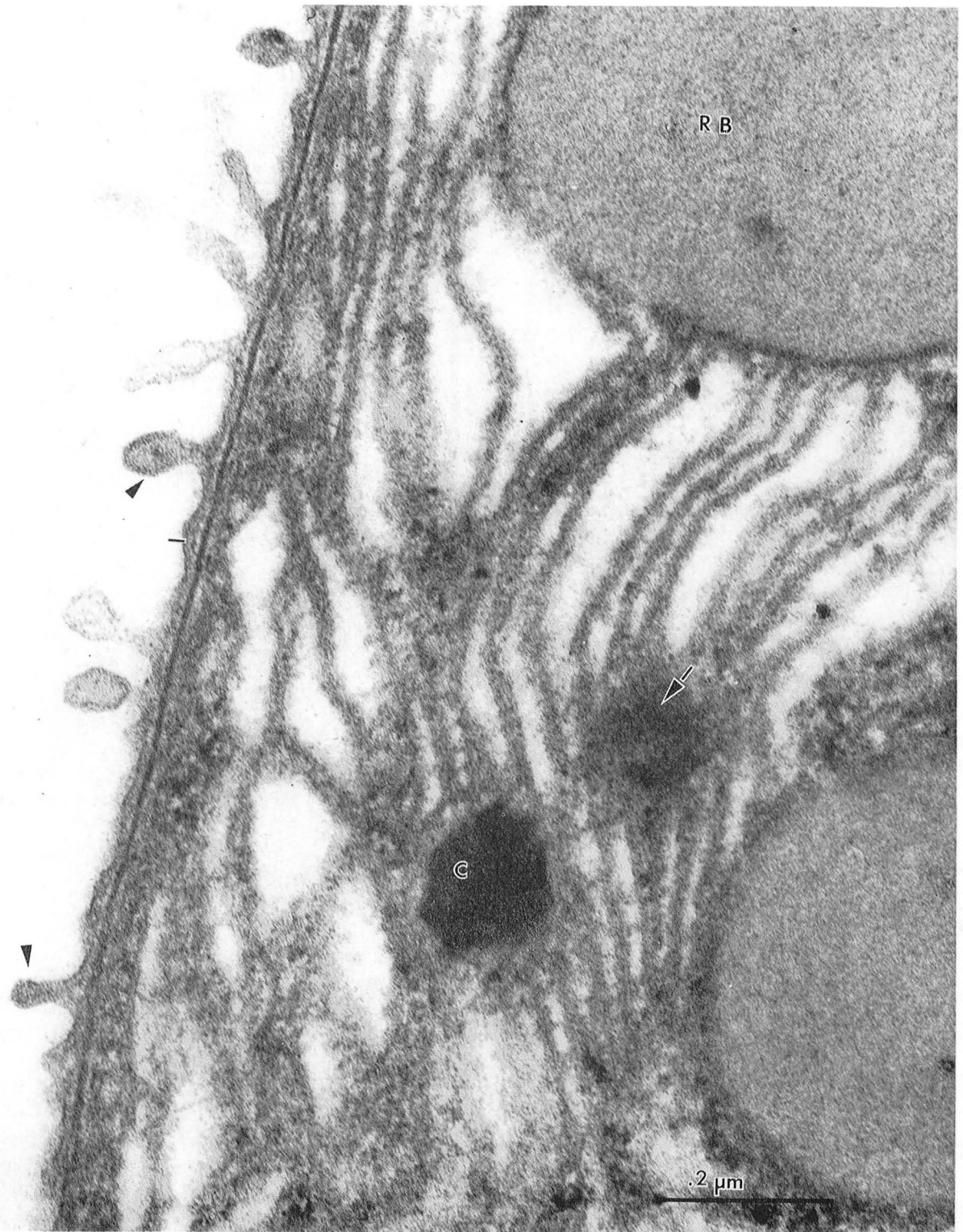


Fig. 37. Prochloron sp. (Prochlorophyta), an ectosymbiont in Didemnum molle, a small tidal animal living in tropical marine waters. Prochloron sp. is a prokaryote of significance to the evolution of life on Earth, because it contains chloroplasts that characterize higher plants. Abbreviations: C - cyanophycin-like inclusion, RB - round body, bar - outer cell wall layer, arrow heads - outer cell wall sculpturations, arrow - group of microtubules.

University concerning the ultrastructure of Prochloron sp., a prokaryotic unicellular alga, placed in a proposed new Division, Prochlorophyta. Prochloron sp. is a peculiar microorganism of evolutionary significance as it has the cytological organization of Cyanobacteriae and has chlorophyll b, a physiological feature of Chlorophytae and higher plants. Therefore this alga may be a link to our understanding of evolution in photosystems.

The samples used in the study were collected on the island of Palau, Micronesia. The cytological study revealed novel ultrastructural details. The outer layer of the cell wall had well-developed protrusions (sculpturations) (Fig. 37). The photosynthetic apparatus was multilayered with a complicated arrangement. The thylakoids were peripherally located and, in some cells, loosely arranged. However, a region always existed along the lamellae where the thylakoids were paired. Some cells had massive stacks of appressed thylakoids, which indicates the location of their PSII.

Different types of cell inclusions and granules were observed. Four basic types of inclusions were classified according to their shape, density, size, location, frequency, and staining properties. Young and old cells showed differences in structure, which indicated that the type and number of inclusions and the complexity of the photosynthetic apparatus depends partially upon the age of the cell. Two new ideas about this paradoxical prokaryotic alga arose from ultrastructural observations: (1) Prochloron sp. from different hosts are actually different species, and (2) Prochloron sp. are pleomorphic organisms (having more than one form during their life cycles).

Director's Discretionary Funding

The nature of scientific inquiry requires freedom for the investigator to explore areas that can supply new insight. Often research in seemingly unrelated areas inspires a practical solution to a pressing problem. Yearly, a Discretionary Fund distributed through the Office of the Director at Ames Research Center offers just such an opportunity for investigators to develop new ideas that are otherwise difficult to initiate, but are essential to future progress. Demanding standards are used to judge proposals on technical and scientific merit, and compatibility with the goals of Ames and NASA. The six-member Ames Basic Research Council, consisting of a representative from each of the technical directorates at Ames, submits funding recommendations to the Center Director twice yearly. Four proposals submitted by the Biomedical Research Division were chosen in FY 1983: (1) Role of Brain Peptides in Motion Sickness by N.G. Daunton, (2) Computer Model of Insulin Resistance during Weightlessness by C.B. Dolkas, (3) Study of Atrophy of Skeletal Muscles in Simulated Weightlessness by H.S. Ginoza, and (4) Physiological Studies of Growth Hormone Releasing Factor by R.E. Grindeland.

Appointments and Awards

M.M. Cohen: Lecturer in Astronautics and Aeronautics, Stanford University, Stanford, CA.

Member, National Research Council/National Academy of Sciences Working Group on Simulator Sickness.

Member, NASA Space Station Crew Systems Safety Study, an informal advisory and review committee.

Member, Space Adaptation Working Panel, which coordinates studies of biological sensory processing on Space Shuttle missions.

N.G. Dauntton: Project Scientist, Vestibular Research Facility (VRF), which is designed to provide motion and visual stimuli in various species for research on the operation of the vestibular system.

Member of Animal Care and Use Committee, Ames Research Center.

Member, Space Adaptation Working Panel, which coordinates studies of biological sensory processing on Space Shuttle missions.

D.J. Goldwater: Clinical Instructor of Medicine and Cardiology, Lecturer and Adjunct Professor of Astronautics and Aeronautics, Stanford University, Stanford, CA.

J.E. Greenleaf: Aerospace Medical Association Award for the best scientific paper, "Hemodilution, vasopressin suppression, and diuresis during water immersion in man," published in Aviation, Space and Environmental Medicine (52: 329-336).

R.E. Grindeland: Chairman, Animal Care and Use Committee, Ames Research Center.

E.M. Holton: Lecturer in Astronautics and Aeronautics, Stanford University, Stanford, CA.

Exceptional Scientific Medal, Ames Research Center, in recognition of her exceptional scientific contributions toward elucidating the effects of spaceflight and hypogravity on the skeletal system.

L.C. Keil: Member, Academic Affairs Committee, Ames Research Center, which reviews proposals from outside institutions.

L.M. Kraft: Member of the Search Committee for Director of Laboratory Animal Medicine, Stanford University, Stanford, CA.

Member of Animal Care and Use Committee, Ames Research Center.

Member of the Administrative Panel on Laboratory Animal Care, Stanford University, Stanford, CA.

A.D. Mandel: Workshop on Cell Culturing and Quality Control, Burlingame, CA.

Member, NASA Space Station Crew Systems Safety Study, an informal advisory and review committee.

W.R. Mehler: Adjunct Professor of Anatomy, University of California at San Francisco.

J. Miquel: Associate Professor of Gerontology, University of Florida at Gainesville.

Adjunct Professor of Toxicology and Environmental Gerontology, San Jose State University, San Jose, CA.

Professor of Gerontology, Alicante University School of Medicine, Murcia, Spain.

Consultant in Gerontology, Linus Pauling Institute of Science and Medicine, Palo Alto, CA.

Editorial Boards: AGE, The Journal of the American Aging Association, Inc.; Archives of Gerontology and Geriatrics; Geriatrika; Mechanisms of Aging and Development; and Revista Espanola de Geriatria y Gerontologia.

Fellow of the American Gerontological Society.

J. Oyama: Member, NASA Variable Gravity Research Facility Advisory Committee to develop requirements for the establishment of a large centrifuge for spaceflight.

Consultant, Swiss National Science Foundation.

Consultant, Regulatory Biology Program, National Science Foundation.

D.E. Philpott: Consultant, Department of Pathology, Presbyterian Hospital, San Francisco, CA.

Consultant, Electron Microscopic Methods and Interpretation, Veteran's Administration Hospital, New York, NY.

Charter and Current Member of the National Board for Certification of Electron Microscopists, Electron Microscope Society of America.

Member of the board to set curriculum requirements for electron microscope technicians, San Joaquin Delta College, Stockton, CA.

Science Coordinator, Students Space Biology Research Program,
Ames Research Center.

Member, NASA Space Station Crew Systems Safety Study, an
informal advisory and review committee.

H. Sandler: NASA's First Senior Executive Services Sabbatical for his
internationally recognized contributions in cardiovascular
research and the biomedical effects of extended duration
spaceflight.

Clinical Professor of Medicine, Stanford University, Stanford, CA.

Adjunct Associate Professor of Medicine, Wright State
University, Dayton, OH.

Consultant, Cardiovascular Research Institute, University of
California at San Francisco.

Consultant, Hypertension Task Force, National Heart and Lung
Institute, National Institutes of Health.

Consultant, Cardiovascular Experimental Study Section,
National Institutes of Health.

Editorial Boards: Aviation, Space and Environmental
Medicine; Circulation Research; Emergency Medicine; and the
Journal of Biotelemetry.

Fellow of the Aerospace Medical Association, American College
of Angiology, American College of Cardiology, Circulation Group
of the American Physiological Society, and the American Heart
Association (Council on Circulation).

M.J. Stevenson: Assistant Science Coordinator, Students Space
Biology Research Program, Ames Research Center.

C.M. Winget: Professor of Pharmacology and Toxicology, Florida
Agricultural and Mechanical University, Tallahassee, FL.

Adjunct Professor of Physiology, Wright State University,
Dayton, OH.

Lecturer in Animal Physiology, University of California,
Davis, CA.

Lecturer in Biological Sciences, San Jose State University,
San Jose, CA.

Consultant, U.S. Olympic Committee, Sports Medicine
Division.

Lectures, Meetings and Workshops

M.M. Cohen: "Enhanced Gz Tolerance through the Use of a Liquid Cooled Garment" presented at the 54th Annual Scientific Meeting of the Aerospace Medical Association, Houston, TX. Also, chaired the Vibration/Ejection Session.

Addressed an advisory panel on Space Station Operational Medicine Considerations, American Institute of Biological Sciences (AIBS) and the American College of Physicians, Washington, D.C.

Met frequently to review Space Shuttle flight experiments with the Space Adaptation Working Panel, Universities Space Research Association, Houston, TX.

B.C. Daligcon: "Increased Gluconeogenesis in Hyper-G Stressed Rats" presented at the American Physiological Society Meeting, San Diego, CA.

N.G. Daunton: Met frequently to review Space Shuttle flight experiments with the Space Adaptation Working Panel, Universities Space Research Association, Houston, TX.

Co-chair of the Mechanisms of Motion-Induced Vomiting Workshop, 12th Annual Meeting of the Society for Neuroscience, Minneapolis, MN.

"Basic Mechanisms of Space Motion Sickness" presented at Stanford University, Stanford, CA.

"Basic Neural Mechanisms of Motion and Space Sickness" presented at Space Down to Earth: The Fourth Annual Workshop for Teacher/Administrator Teams, Ames Research Center.

C.B. Dolkas: Workshop in Pathophysiological Studies by Nuclear Magnetic Resonance (NMR) in vivo Spectroscopy, Society of Magnetic Resonance, Berkeley, CA.

Attended the Second Annual Scientific Meeting of the Society of Magnetic Resonance in Medicine, San Francisco, CA.

S. Ellis: Advised an ad hoc committee on Muscle Atrophy Associated with Spaceflight, Life Sciences Research Office, Federation of American Societies for Experimental Biology (FASEB), Bethesda, MD.

Attended the Second Annual Scientific Meeting of the Society of Magnetic Resonance in Medicine, San Francisco, CA.

H.J. Ginoza: "Factors Affecting Atrophy of Load Bearing Muscles of Rats in Simulated Weightlessness" presented at the American Physiological Society Meeting, Honolulu, HI.

D.J. Goldwater: "Weightless Simulation" presented at the 54th Annual Scientific Meeting of the Aerospace Medical Association, Houston, TX.

"Hematuria Following Hypergravic Exposure in Middle-aged Women" presented at the American Physiological Society Meeting, San Diego, CA.

Attended the Annual Meeting of the American Heart Association, Dallas, TX.

J.E. Greenleaf: "Body Temperature Increases to Repeated Exercise in Dogs: Adrenergic Implications" presented at the American Physiological Society Meeting, Honolulu, HI.

"Bedrest Studies: Fluid and Electrolyte Responses" presented at the Space Physiology Symposium, Toulouse, France.

R.E. Grindeland: "Differential Secretion of Bioassayable Growth Hormone by Two Types of Rat Somatotrophs" presented at the American Physiological Society Meeting, San Diego, CA.

E.M. Holton: Workshop on Morphological Aspects of Bone Biology, Sun Valley, ID.

"Is Suppression of Bone Formation during Simulated Weightlessness Gradual and Related to Glucocorticoid Levels?" presented at the Annual Meeting of the International Union of Physiological Sciences (IUPS) Commission on Gravitational Physiology, San Diego, CA.

Workshop on NASA Life Sciences Requirements for Space Station, Leesburg, VA.

L.M. Kraft: "A Natural Poxvirus Infection of Rats: Morphological Evidence in Spaceflight Experimental Animals" presented at the Annual Meeting of the American Association for Laboratory Animal Science, Washington, D.C.

Workshop on Mechanisms of Motion-Induced Vomiting, 12th Annual Meeting of the Society for Neuroscience, Minneapolis, MN.

W.R. Mehler: Co-chair of the Mechanisms of Motion-Induced Vomiting Workshop, 12th Annual Meeting of the Society for Neuroscience, Minneapolis, MN.

D.E. Philpott: (1) "External Morphology of Shuttle Flown Worker Bees as Shown by Scanning Electron Microscopy," (2) "The Use of a

Ruled Reticle for Stereology Directly Off the Fluorescent Screen," and (3) "An Image Storage and Computer System for Statistical Analysis" presented at the 11th Annual Western Regional Meeting of Electron Microscopists, Asilomar, CA.

"The Response of a Mixed Cell Population in Mouse Testes to X-ray and HZE Irradiation" presented at the Joint Meeting of the Electron Microscope Society and the Microbeam Analysis Society, Phoenix, AZ.

H. Sandler: "Medical Benefits of Spaceflight" presented at the Clinical Care Convocation, Oregon Health Sciences University, Portland.

Chair of the Space Medicine Session, 54th Annual Scientific Meeting of the Aerospace Medical Association, Houston, TX.

"Are There Limits to Man's Long-term Presence in Space?" presented at the 13th Intersociety Conference on Environmental Systems, San Francisco, CA.

Attended the Annual Meeting of the American Heart Association, Dallas, TX.

K.A. Souza: Workshop on Future Life Sciences Flight Experiments, NASA Headquarters, Rosslyn, VA.

"Status of Joint US-USSR Experiments Planned for Cosmos 1983 Biosatellite Mission" presented at the 33rd Annual Meeting of the American Physiological Society, San Diego, CA.

M.J. Stevenson: "Data Management for Tissue Samples in an Ultrastructure Laboratory" presented at the Eleventh Western Regional Meeting of Electron Microscopists, Asilomar, CA.

J.A. Williams: "Simulated Weightlessness and Interferon Induction in the Rat" presented at the American Society of Microbiology Meeting, San Francisco, CA.

Workshop on the Latest Procedures of Monoclonal Antibody Technology, Sloan-Kettering Memorial Hospital, New York, NY.

Workshop on Cell Culturing and Quality Control, Burlingame, CA.

C.A. Winget: "Physiological Rhythms in Healthy Adults" presented at American College of Sports Medicine, U.S. Olympic Committee, Montreal, Canada.

"Changes in Waveform and Periodicity of Circadian Body Temperature Rhythm Following Photoperiod Alteration" presented at the 54th Annual Scientific Meeting of the Aerospace Medical Association, Houston, TX.

D.R. Young: Advised an ad hoc committee on Bone Demineralization Associated with Spaceflight, Life Sciences Research Office, Federation of American Societies for Experimental Biology (FASEB), Bethesda, MD.

"The Effects of Immobilization on Cortical Bone in Monkeys (M. nemestrina)" presented at the Fifth Annual Meeting of the International Union of Physiological Sciences (IUPS) Commission on Gravitational Physiology, Moscow, USSR.

Organized a special session on the nonhuman primate model, Workshop on Morphological Aspects of Bone Biology, Sun Valley, ID.

"Acid-base Status during Short-term Immobilization in Monkeys (M. nemestrina)" presented at the American Physiological Society Meeting, Honolulu, HI.

Thesis Committees

N.G. Daunton: Meryl Lee Corcoran, CHARACTERISTICS OF ROTATION TOLERANCE THRESHOLDS IN MONKEYS UNDER ESCAPE-AVOIDANCE PROCEDURES, M.A. in Psychology, San Jose State University.

Linda Diaz, THE ROLE OF EXOGENOUS VASOPRESSIN DURING MOTION SICKNESS IN CATS, M.A. in Psychology, San Jose State University.

Andrea H. Lauber, ALTERED GRAVITY PARABOLIC FLIGHT STIMULATION PRODUCES ANOREXIA AND CONDITIONED TASTE AVERSION IN RATS, M.A. in Psychology, San Jose State University.

Martha McCarty, THE EFFECTS OF VISUAL AND VESTIBULAR LINEAR MOTION ON A POSTURAL ORIENTATION RESPONSE IN PIGEONS, M.A. in Psychology, San Jose State University.

Richard L. Sutton, THE EFFECT OF AREA POSTREMA LESIONS ON DEVELOPMENT OF MOTION-INDUCED CONDITIONED TASTE AVERSIONS IN RATS, M.A. in Psychology, San Jose State University.

J.E. Greenleaf: Nancy Wong, EFFECT OF ARM EXERCISE ON VENOUS BLOOD CONSTITUENTS DURING LEG EXERCISE, M.S. in Physiology, San Francisco State University.

William A. Spaul, PHYSIOLOGICAL EFFECTS OF COMBINED EXPOSURE TO HEAT STRESS AND VIBRATION, Ph.D. in Public Health, University of California at Berkeley.

Christine A. Elder, PERIPHERAL BLOOD FLOW AND THERMOREGULATORY RESPONSES DURING HEATING IN MAN, M.S. in Physiology, San Francisco State University.

E.M. Holton: A. Christopher Maese, BONE FORMATION RATE IN LONG BONES ON TWO STRAINS OF RATS FROM ONE THROUGH EIGHT MONTHS OF AGE, M.S. in Biology, San Jose State University.

J. Oyama: Conrad Monson, MECHANISMS OF THERMOREGULATION IN RATS EXPOSED TO HYPERGRAVIC FIELDS, Ph.D. in Animal Physiology, University of California at Davis.

June L. Glenn-Lawson, STUDIES ON THE USE OF ISOLATED HEPATOCYTES TO DETERMINE THE EFFECTS OF HYPERGRAVITY EXPOSURES ON GLUCONEOGENESIS IN RATS, M.S. in Biological Sciences, San Jose State University.

Seminar Speakers Invited by the Biomedical Research Division in FY 1983

Dr. Charles M. Tipton, Departments of Physical Education, Physiology and Biophysics, University of Iowa

EXERCISE: SHOULD IT BE CONSIDERED AS A COUNTERMEASURE FOR MANNED SPACEFLIGHTS?

Dr. Stephen D. Rosen, Department of Anatomy, University of California School of Medicine

MOLECULAR MECHANISMS OF INTRACELLULAR ADHESION IN SLIME MOLDS AND HIGHER ORGANISMS

Dr. A. Guell, Groupe de Recherche sur la Circulation Cerebrale, Service de Neurologie, France

EFFECTS OF CLONIDINE DURING BEDREST

Drs. I. B. Kozlovskaya, L. V. Serova, A. A. Shipov, and A. S. Ushakov, Institute of Biomedical Problems, Moscow

VARIOUS ASPECTS OF SOVIET RESEARCH IN SPACE BIOLOGY AND MEDICINE

Dr. Peter Nagainis, Department of Biochemistry, University of Arizona

THE CALCIUM-ACTIVATED PROTEASE AND MUSCLE PROTEIN TURNOVER

Dr. Frank E. Stockdale, Department of Medicine, Stanford University

ASPECTS OF SKELETAL MUSCLE DEVELOPMENT

Dr. Peter K. T. Pang, Department of Pharmacology, Texas Tech University

THE VASCULAR ACTIONS OF PARATHYROID HORMONE

Dr. V. Reggie, Edgerton, University of California at Los Angeles

FACTORS RELATIVE TO MUSCLE ATROPHY AND FATIGUE

Dr. Kenneth R. Brizzee, Delta Primate Research Center, Tulane University

MORPHOPHYSIOLOGY OF THE AREA POSTREMA

THE VOMITING CENTER REVISITED

Dr. Makoto Igarashi, Department of Otorhinolaryngology, Baylor College of Medicine

VESTIBULAR-VISUAL CONFLICT SYMPTOMS IN THE SQUIRREL MONKEY

Dr. Herbert L. Borison, Department of Pharmacology, Dartmouth Medical School

NEUROPHARMACOLOGY OF VOMITING

Dr. Christopher Coe, Department of Psychiatry, Stanford University Medical Center

BIOLOGY OF THE SQUIRREL MONKEY AND ITS USE IN MEDICAL RESEARCH

Dr. DeSales Lawless, NASA/Stanford Summer Faculty Fellow

USE OF LIPOSOME CONTAINING MONOCLONAL ANTIBODIES TO DETECT T-CELL SUBSETS

Dr. Lawrence Schwartz, University of Washington School of Medicine
HORMONAL CONTROL OF SKELETAL MUSCLE DEGENERATION IN AN INSECT

Dr. George Crampton, Department of Psychology, Wright State University
ROLE OF CATECHOLAMINES IN MOTION SICKNESS IN CATS

Dr. Arnon Rolnick, Spatial Orientation Laboratory, Brandeis University
ACTIVE VS. PASSIVE MOTION AND ITS RELATIONSHIP TO MOTION SICKNESS IN RATS
AND HUMANS

Dr. Jacob Zabara, Department of Physiology, Temple University
INHIBITION OF EMESIS AND NAUSEA

Dr. Thomas Harrington, Department of Psychology, University of Nevada
VISUAL ORIENTATION

FACILITIES

FACILITIES

Ames Research Center has facilities that are unique throughout the world for the study of biomedical issues in aerospace medicine and gravitational biology. Many of these facilities simulate the aerospace environment for investigators to study the biological effects of simulated weightlessness, acceleration, and even the rarified atmosphere of other planets. While the aeronautical facilities give Ames the reputation as "a city of wind tunnels," it is also "a city of centrifuges," which are used in both animal and human biological research. Tables and descriptions follow of the many specialized facilities at Ames used by investigators of the Biomedical Research Division.



Fig. 38. One of the Life Sciences Research Laboratories at Ames Research Center, housing some of the unique facilities of the Biomedical Research Division.

TABLE IV. FACILITIES MANAGED BY BIOMEDICAL RESEARCH DIVISION (LR)

<u>FACILITY</u>	<u>DESCRIPTION</u>
Cardiovascular Research Laboratory (Bldg. 236)	
Surgical Suite	Used in the preparation of animals for biomedical research.
X-ray Room	X-ray studies of the heart and blood vessels, using radioactive tracers and high speed film.
Angiography Suite	Radiological study of the heart and blood vessels.
Animal Water Immersion Facility	Used to reproduce many of the physiological changes accompanying microgravity.
Bioinstrumentation Lab	Develop and test advanced biomedical electronic equipment.
Data Processing Room	PDP 11/34 computer.
Neurosciences Laboratory (Bldg. 239)	
Surgical Area	Used in the preparation of animals for research of the anatomy and neural pathways affecting motion sickness.
Sensory Conflict Test Chambers	Test animal subjects using visual stimulation and physical agitation to establish visual and vestibular cues in motion sickness.
Data Processing	PDP 11/34 computer.
Psychophysiology Laboratory (Bldg. 239-A)	
Biofeedback Test Chambers	Used to train humans in self-control of motion sickness symptoms during visual stimulation and physical agitation.
Data Processing	PDP 11/34 computer.

Bone Physiology Laboratories (Bldgs. 236 and 239, three labs)

Bone Biomechanics Area	Research to measure bone strength and mechanisms of disuse osteoporosis.
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Bone Image Analysis System	Program on PDP 11/34 digitizes bone images to trace chemical labels quickly.
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Animal Centrifuges (Bldg. 239-A)	8, 24 and 52 ft diameter centrifuges for short and chronic testing of gravity-sensitive biological systems.
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Electron Microscopy Laboratory (Bldg. 239)	Conduct morphological studies of animal ultrastructures using two transmission electron microscopes, scanning electron microscope, and specialized tissue processing equipment.
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Immunology/Tissue Culture Laboratory (Bldg. 239-A)	Clean room for growing tissue cultures.
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Human Environmental Physiology Laboratory (Bldg. 239-A)

Human Water Immersion Tank	Used to simulate physiological alterations accompanying weightlessness in humans.
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Environmental Test Facility	Perform psychological and physiological tests on humans during isolation, exercise, and changes in temperature, pressure and humidity.
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Animal Biorhythm Laboratory (Bldg. 239)

Environmental Test Chambers	Monitor animal responses to changes in temperature, pressure and humidity.
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Histochemistry/Histopathology Laboratories (Bldgs. 236 and 239)	Two labs to study vestibular function and radiation biology.
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Biochemistry/Endocrinology
Laboratories

Six labs to study fluid and electrolyte biochemistry, and muscle biochemistry.

General Physiology Laboratories (Bldg. 239, five labs)

Vertical Acceleration and Roll
Device (VARD) (Bldg. 239-A)

Human test simulator used in studies of spaceflight physiological changes, including tests for space motion sickness.

Trailers

Eleven trailers as temporary laboratory facilities.

TABLE V. RESEARCH FACILITIES USED BY LR AND MANAGED BY OTHER ORGANIZATIONS

<u>FACILITY</u>	<u>DESCRIPTION</u>
Human Research Facility (Bldg. 236)	Used to conduct human bedrest studies; managed by Biosystems Division, Life Sciences Directorate.
Human Centrifuge (Bldg. 221-A)	50 ft diameter, 20-G centrifuge; managed by Flight Systems and Simulation Research Division, Aeronautics and Flight Systems Directorate.
Man Carrying Rotation Device (Bldg. 239-A)	Evaluate performance of pilots and potential Shuttle passengers during physical agitation; managed by Flight Systems and Simulation Research Division, Aeronautics and Flight Systems Directorate.
Animal Colony (Bldg. 236)	Housing for test animals; managed by Biosystems Division, Life Sciences Directorate.
Ames Learjet	Parabolic flight and motion sickness experiments; managed by Airborne Missions and Applications Division, Astronautics Directorate.
Electro-Systems Engineering Branch (Bldg. 213)	Design and engineer bioinstrumentation for spaceflight and ground studies; managed by Research Facilities and Instrumentation Division, Research Support Directorate.
Bevalac (U.C. Berkeley)	Linear accelerator that produces heavy particles (similar to cosmic ray particles) to test effects on animals; managed by Lawrence Berkeley Laboratories at the University of California, Berkeley.

ANIMAL CENTRIFUGES

Animal studies using centrifuges are a specialty of the Biomedical Research Division. Such experiments determine the biological effects of different degrees of gravitational force. Investigators can also identify acceleration effects to differentiate them from the weightlessness effects of spaceflight.

A 2.44m dia animal centrifuge is used with small laboratory animals for acute exposures to hypergravity up to 24 hrs in duration. This centrifuge provides a 10 G field, but most studies do not exceed 5 G. Each of ten radial arms supports at least one cage assembly, and some hold two. The minimum radius to test specimens is approximately 457 mm and the maximum radius is approximately 1.68m. Both rectal and tail temperatures of 18 rats can be monitored simultaneously. A thermally controlled holding cage, or metabolic chamber, can monitor the rate of oxygen consumption and carbon dioxide production from an individual rat during centrifugation.

7.31m dia chronic animal centrifuge (Fig. 39) is used primarily with small laboratory animals for long-term exposures to hypergravity up to three years. Each of ten radial arms supports two cages at an inner and an outer position. The centrifuge operates continuously, except for service stoppages twice weekly to change sawdust-lined cages and replenish the feed. water is available at all times through an automated, nuzzle valve watering system. The animals are subjected to the resultant of the centrifugal and graviational forces as the cages swing outward when the centrifuge is operating. The centrifuge speed is 26.1 revolutions per minute (rpm), which subjects animals at the outer position to 3.1 G and to 2.1 G at the inner position. Each suspended cage can hold six standard sized rat cages. Normally, a maximum of two adult rats per cage is used in chronic studies, for a total of 240 rats at one time. Non-centrifuged control rats are maintained under normal gravity in the centrifuge room to ensure that they are subjected to the same amount of noise, light (12 hrs on/12 hrs off), and handling as the centrifuged rats.

Fig. 40 shows an interior view of the 15.85m dia continuous animal centrifuge. the platform of the centrifuge supports ten radial tracks, where one or two cage assemblies are positioned. Each cage assembly has its own waste removal system, and water and feed delivery system, which permits continuous operation of the centrifuge for the indefinite periods of time. The centrifuge has operated for two months without any stoppage. With a maximum speed of 20 rpm the centrifuge can generate 3 G at the outermost position. An onboard television camera and videotape system can monitor and prduce visual records of the physical activity of centrifuged animals. Heart rate and deep body temperatures have been recorded from various species of animals, such as rats, rabbits and dogs, during chronic centrifugation. This centrifuge is unique in providing laboratory animals with long-duration, continuous exposures to hypergravity.

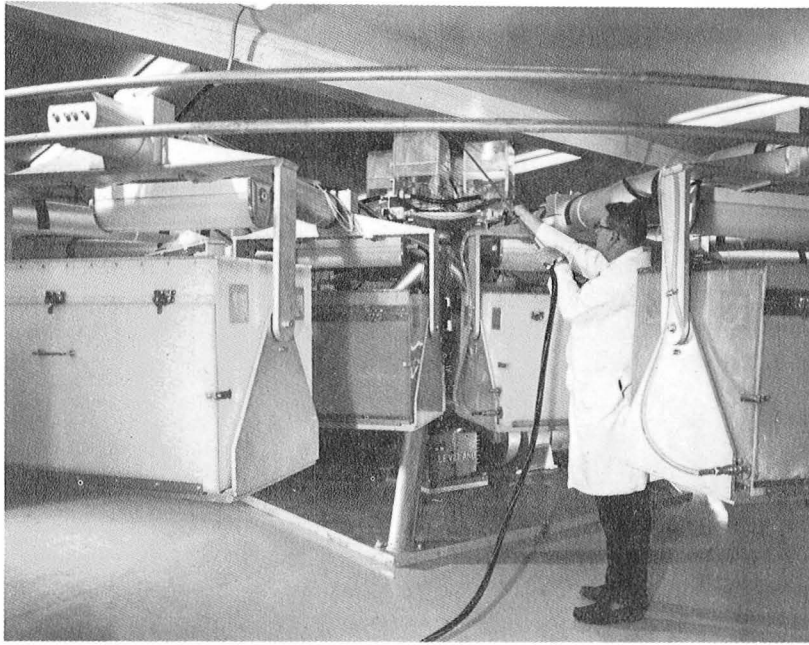


Fig. 39

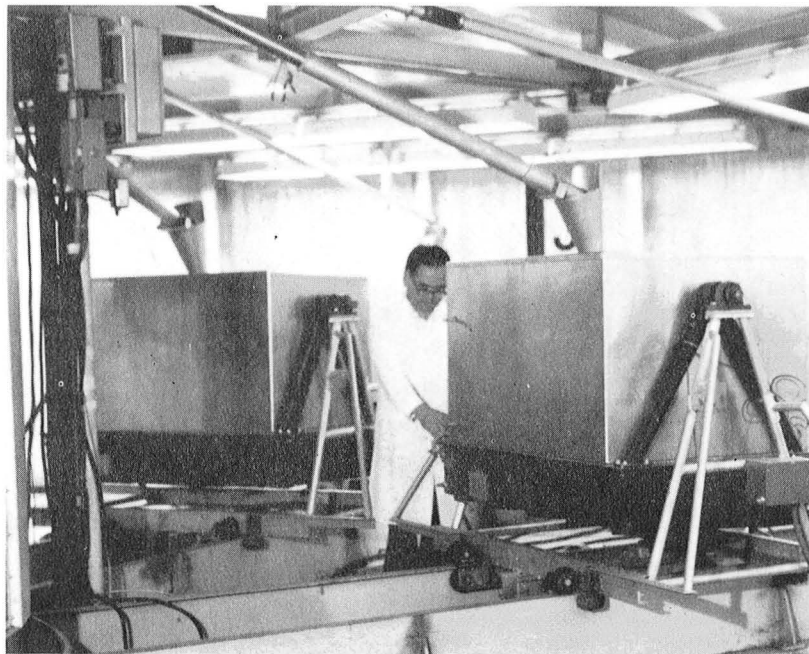


Fig. 40

20-G HUMAN CENTRIFUGE

The 20-G Human Centrifuge (Fig. 41) at Ames is the only facility of its kind in NASA. Investigators use the 20-G centrifuge to examine the effects of G-forces on biological subjects, specimens and instrument packages to determine their qualification for flight. This facility is especially useful in basic research studies of reactions, relating to the stress of reentry in flights of the Space Shuttle, by both astronauts and cross sections of the population at large. Such studies establish criteria to provide the optimum health and safety for space travellers under the Operational Medicine Program.

Continuous centrifugation has been accomplished at this facility for 27 days at 2.5 G, useful for long-term biological experiments, and for more than 20 days at 16 G for hardware testing. The centrifuge has cabs at both ends to hold a maximum payload of 7,257 G kg at each end, e.g., 558 kg at 13 Gs or 362 kg at 20 Gs. The arm radius is 7.62m. Additional equipment weighing up to 907 kg can be mounted within 1.22m of the center of rotation. (Managed by Ames Flight Systems and Simulation Research Division, Aeronautics and Flight Systems Directorate.)

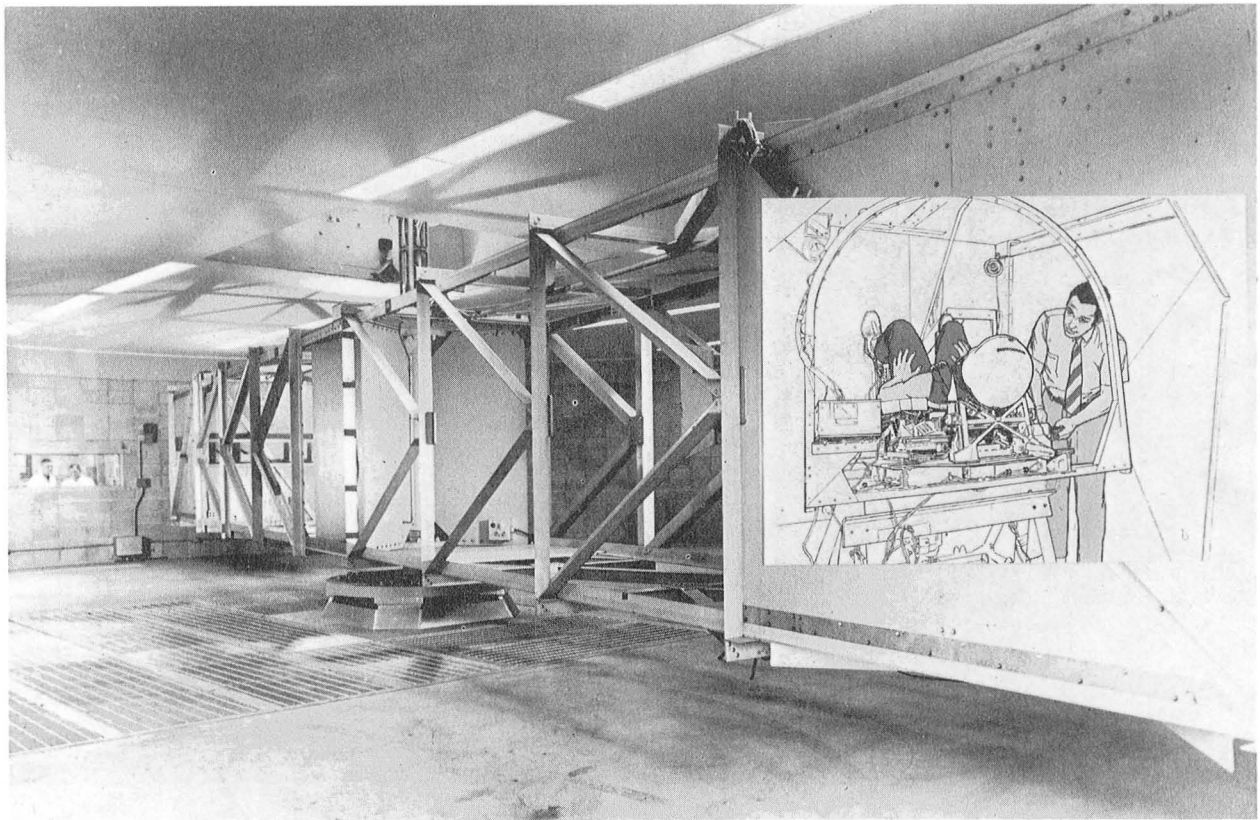


Fig. 41

HUMAN ENVIRONMENTAL PHYSIOLOGY LABORATORY

This laboratory allows LR researchers to provide various physical stresses for the study of human adaptability to altered environmental conditions and simulated weightlessness. Facilities include three environmental chambers (129.5 m^3 , 32.5 m^3 and 18.4 m^3) with controls for heating, cooling and pressure, a tilt table, exercise capacity testing equipment (treadmill and ergometers), and two water immersion tanks (4.0 m^3 and 2.3 m^3). The smaller tank has a scale for measurement of body density.

Two large environmental chambers are used for more specialized studies of humans in a space environment. Both chambers can provide almost any atmospheric gas composition, which is useful in testing optimal mixtures of gases for breathing inside spacecraft. The smaller chamber is especially useful in studying the physiological and psychological responses of human subjects to the stresses of exercise or confinement. The two-story, 129.5 m^3 chamber (Fig. 42) is suited for tests of pressure suits and long-term studies of humans in a spacecraft environment. Both chambers have television monitors and voice intercommunication systems to a control room. Exercise equipment can be accommodated in both chambers. This facility can also support research involving closed ecological systems.

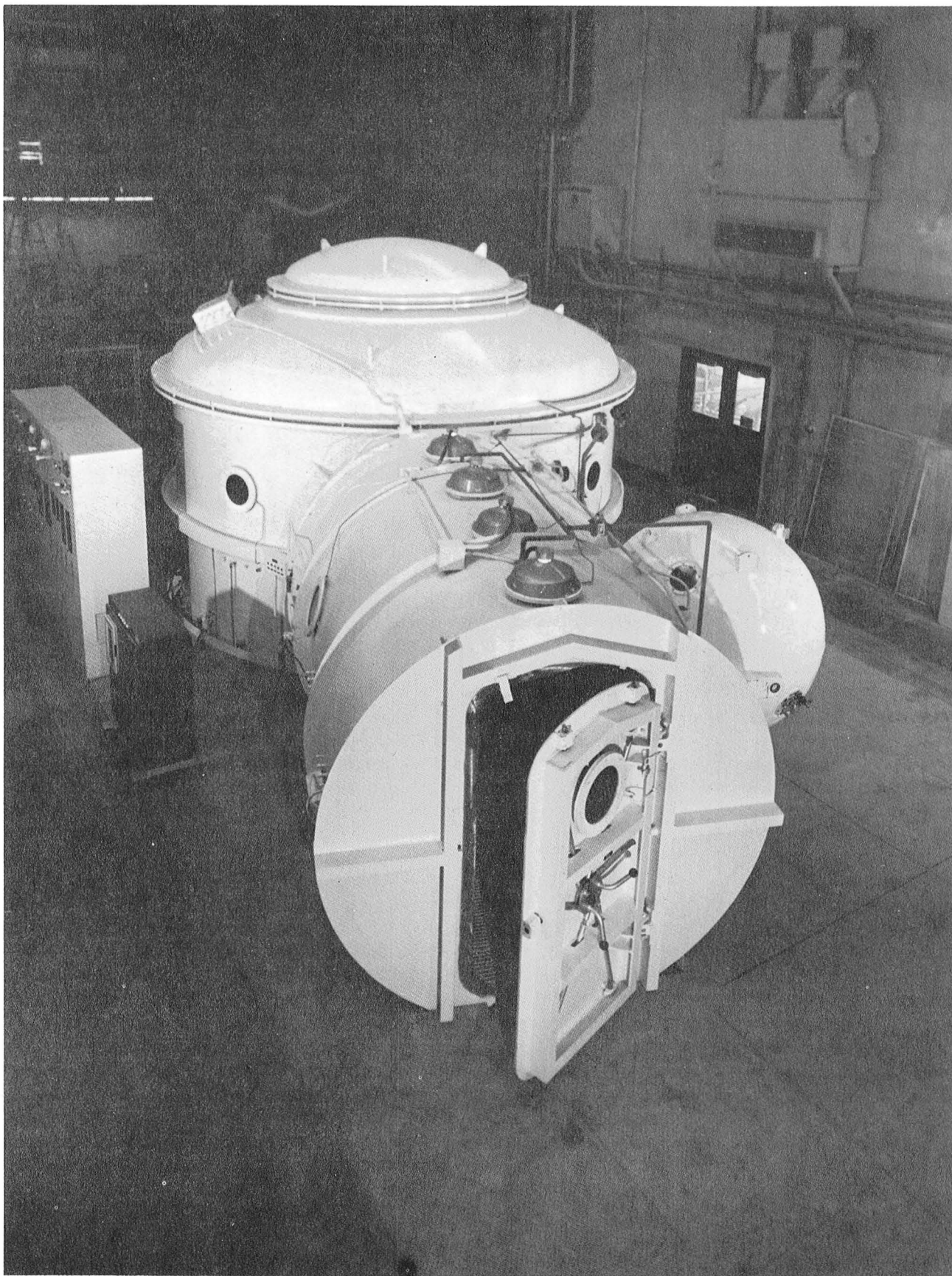


Fig. 42

HUMAN RESEARCH FACILITY

The Human Research Facility can accommodate up to 12 subjects during bedrest simulations of weightlessness, as well as other physiological testing and medical monitoring (Figs. 43 and 44). Basic research studies have been conducted here in support of both the Operational Medicine and Biomedical



Fig. 43

Research Programs. Studies examine the effects of weightlessness on living in space and the efficient operation of aircraft. A unique feature is a horizontal shower for subjects to maintain normal hygiene during bedrest studies of a week or longer. (Managed by Biosystems Division.)



Fig. 44

ELECTRON MICROSCOPY LABORATORY

This facility is equipped with a scanning electron microscope (SEM), which produces pictures of the surface topography of specimens with a remarkable illusion of three-dimensionality. The SEM can magnify the surface of an object more than 100,000x with a superior depth of field.

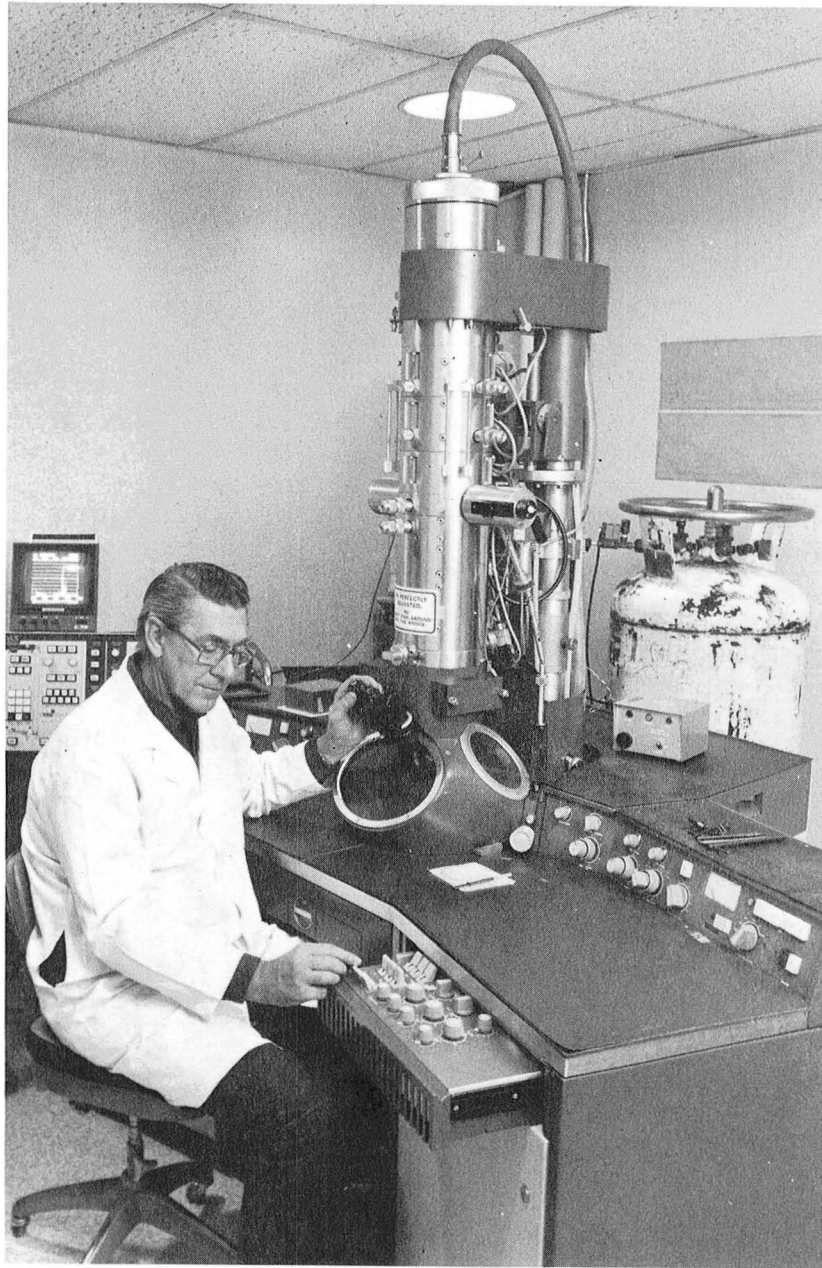


Fig. 45

Whereas a light microscope can focus only on one horizontal plane of a specimen, the SEM scans the entire surface uniformly. Two transmission electron microscopes, like the one in Fig. 45, produce pictures with very high contrast. Specialists in this facility have developed equipment and techniques for processing specimens for viewing. Morphological studies support numerous research efforts including, atrophy effects on cardiac and skeletal muscle, change in the number of receptors for steroids in target cells of the kidney, effects of radiation on neural and optical tissue, and morphological effects on animals flown on the Space Shuttle and Cosmos biosatellites, to name only a few.

LEAR 24B AIRCRAFT

The Lear 24B aircraft (Fig. 46) is a modified, twin-engine executive jet manufactured by Gates Learjet Corporation. This aircraft is used both as a high-altitude observation platform, and weightless simulator for brief periods during parabolic flight. Numerous studies into the cause of space motion sickness with both humans and animals (Fig. 47) have been conducted using the Lear Jet. It has a practical operating range of about 3,704 km at a 241.7 m per sec indicated airspeed, an operating ceiling of about 13.7 km and a useful payload of 453 kg. (Managed by Ames' Airborne Missions and Applications Division, Astronautics Directorate.)



Fig. 46

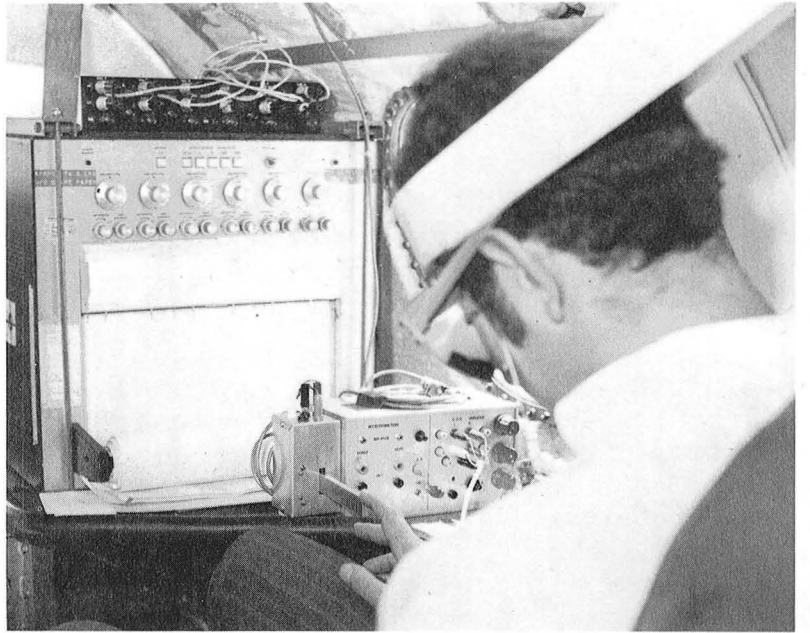


Fig. 47



PSYCHOPHYSIOLOGY LABORATORY

The Psychophysiology Laboratory is used to conduct basic research into the use of biofeedback to counteract undesirable effects of space-flight, such as motion sickness, through learned control of cardio-vascular and other bodily functions. One booth houses a bioinstrumented rotating chair surrounded by a rotating drum to produce optokinetic stimulus (Fig. 48). This system is used to induce Coriolis and pseudo-Coriolis acceleration in human subjects while monitoring their physiology. The second booth is the primary environment to administer Autogenic-Feedback Training to combat aerospace motion sickness. The environment is designed to induce complete relaxation in subjects while they undergo specific training procedures without distractions from outside activities. It contains a wide variety of biomedical equipment connected to an elaborate system, which outputs signals directly from the subject to the main lab for analysis, and immediately feeds specific information back for use by the trainer and the subject.



Fig. 48

VERTICAL ACCELERATION AND ROLL DEVICE (VARD)

The Vertical Acceleration and Roll Device (Figs. 49 and 50) is a dynamic flight simulator used for aircraft human factors studies, as well as for biomedical investigations that require vertical accelerations. It consists of a two-place, side-by-side cockpit supported on a vertical track. This simulator is normally driven open loop. It can be operated closed loop with flight dynamics generated on an analog or digital computer programmed to account for dynamic response of the vehicle to control inputs from the pilot. The VARD has proven useful in experiments on motion sickness.

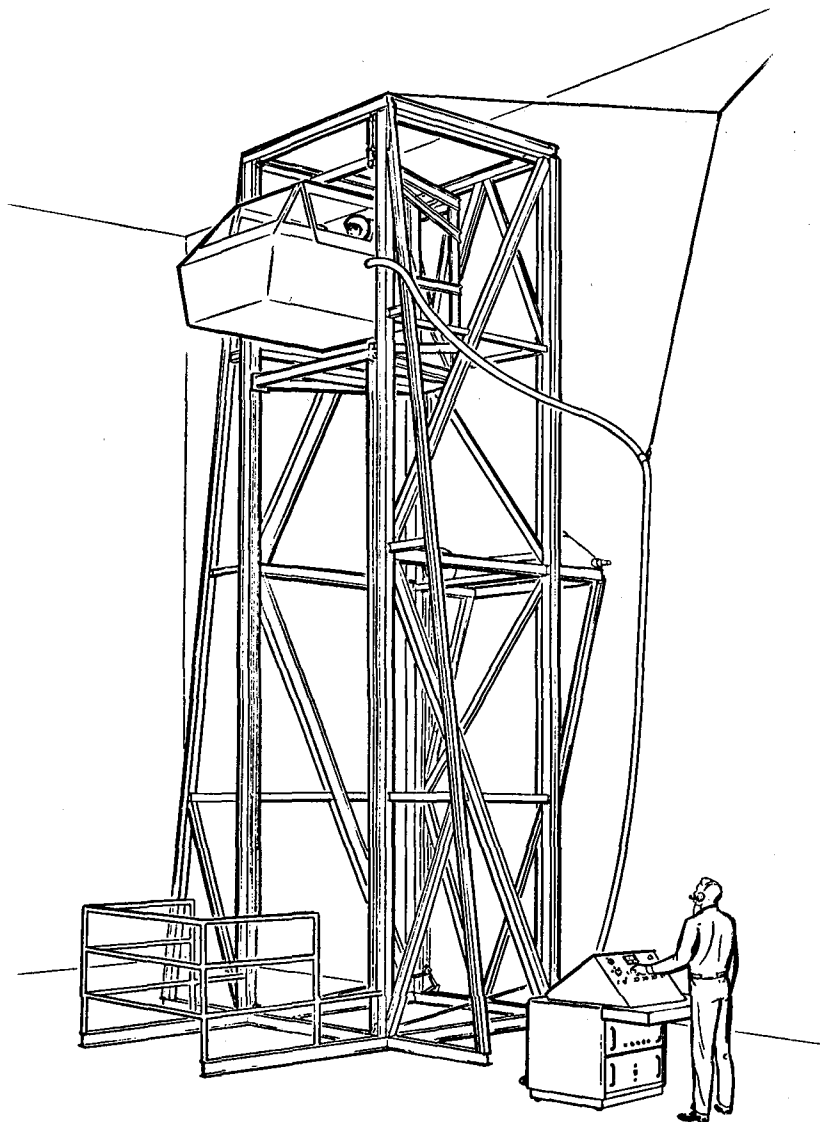


Fig. 49

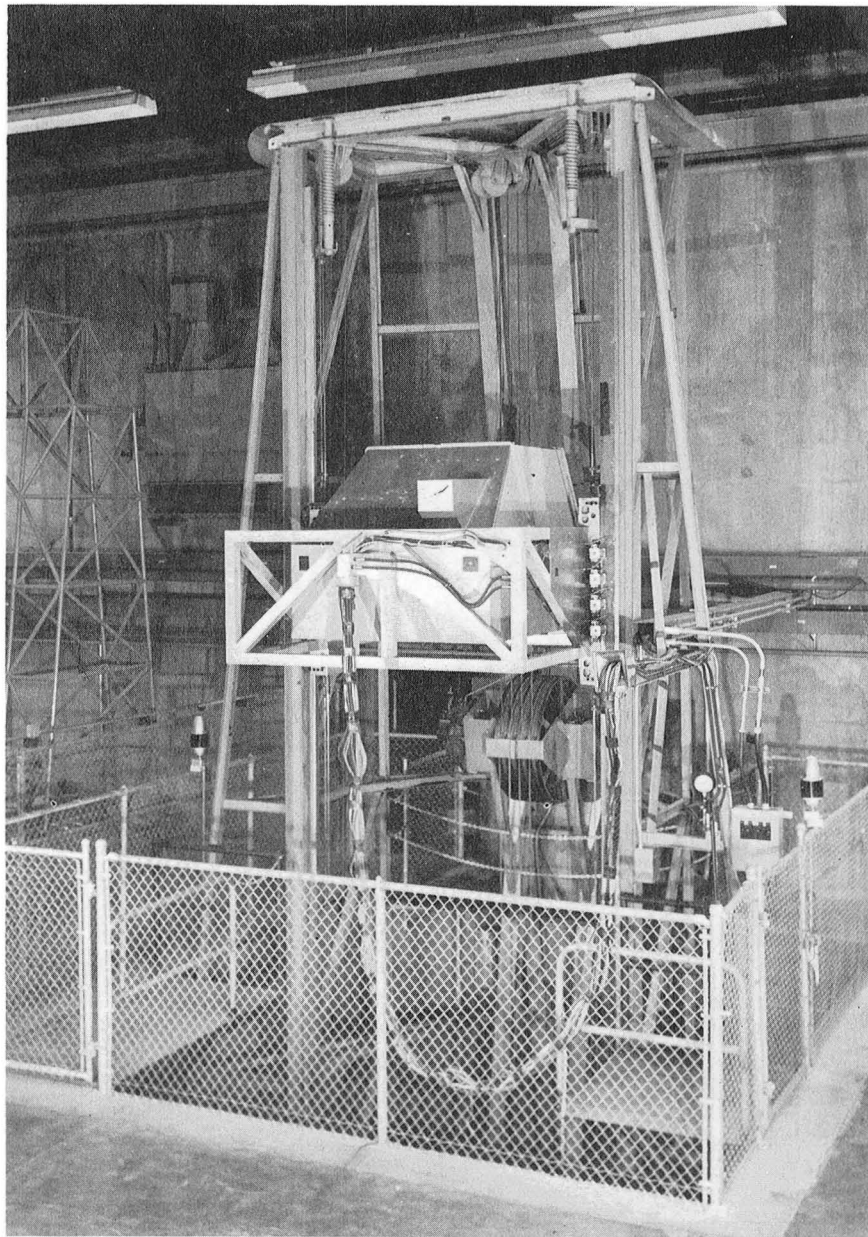


Fig. 50

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16. Abstract This report describes various research and technology activities at Ames Research Center's Biomedical Research Division. Contributions to the Space Administration's goals in the life sciences include research in operational medicine, cardiovascular deconditioning, motion sickness, bone alterations, muscle atrophy, fluid and electrolyte changes, radiation effects and protection, human behavior and performance, general biomedical research, and gravitational biology.			
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